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EUROPEAN HEALTH AND DIGITAL EXECUTIVE AGENCY (HADEA)

HADEA.A – Health and Food
A.3 – Health research

GRANT AGREEMENT

Project 101156595 — ERDERA

PREAMBLE

This **Agreement** ('the Agreement') is **between** the following parties:

on the one part,

the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and

on the other part,

1. 'the coordinator':

INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM), PIC 999997833, established in RUE DE TOLBIAC 101, PARIS 75654, France,

and the following other beneficiaries, if they sign their 'accession form' (see Annex 3 and Article 40):

2. **TEAMIT RESEARCH SL (TEAMIT)**, PIC 896104237, established in PASSE DE GRACIA 58 PLANTA 4 PUERTA 2, BARCELONA 08007, Spain,

3. **DEUTSCHES ZENTRUM FUR LUFT - UND RAUMFAHRT EV (DLR)**, PIC 999981731, established in LINDER HOHE, KOLN 51147, Germany,

4. **AGENCE NATIONALE DE LA RECHERCHE (ANR)**, PIC 998711613, established in 86 RUE REGNAULT, PARIS 75013, France,

5. **FONDAZIONE TELETHON ETS (FTELE)**, PIC 999448716, established in VIA VARESE 16/B, ROMA 00185, Italy,

6. **Lietuvos mokslo taryba (LMT)**, PIC 997808446, established in Gedimino 3, Vilnius LT-01103, Lithuania,

7. **ZORGONDERZOEK NEDERLAND ZON (ZonMw)**, PIC 999544164, established in Laan Van Nieuw Oost Indie 334, DEN HAAG 2593 CE, Netherlands,

8. **EBERHARD KARLS UNIVERSITAET TUEBINGEN (UT)**, PIC 999991916, established in GESCHWISTER-SCHOLL-PLATZ, TUEBINGEN 72074, Germany,

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9. **TARTU ULIKOOL (UTARTU)**, PIC 999895013, established in ULIKOOLI 18, TARTU 50090, Estonia,

10. **CONSORCIO PARA LA EXPLOTACION DEL CENTRO NACIONAL DE ANALISIS GENOMICO (CNAG)**, PIC 882802433, established in C BALDIRI 1 REIXAC 4, BARCELONA 08028, Spain,

11. **STICHTING RADBOUD UNIVERSITAIR MEDISCH CENTRUM (SRUMC)**, PIC 892057785, established in GEERT GROOTEPLEIN 10 ZUID, NIJMEGEN 6525 GA, Netherlands,

12. **TECHNISCHE UNIVERSITAET MUENCHEN (TUM)**, PIC 999977463, established in Arcisstrasse 21, MUENCHEN 80333, Germany,

13. **UNIVERSITATSKLINIKUM HEIDELBERG (UKHD)**, PIC 999841081, established in IM NEUENHEIMER FELD 672, HEIDELBERG 69120, Germany,

14. **CRITICAL PATH INSTITUTE STICHTING (C-PATH)**, PIC 887895418, established in BARBARA STROZZILAAN 101, AMSTERDAM 1083 HN, Netherlands,

15. **FUNDACIO HOSPITAL UNIVERSITARI VALL D'HEBRON - INSTITUT DE RECERCA (VHIR)**, PIC 999541642, established in PASSEIG VALL D HEBRON 119-129 EDIFICIO DE RECERCA, BARCELONA 08035, Spain,

16. **ACADEMISCH ZIEKENHUIS LEIDEN (LUMC)**, PIC 999990849, established in ALBINUSDREEF 2, LEIDEN 2333 ZA, Netherlands,

17. **UNIVERSITEIT TWENTE (UTWENTE)**, PIC 999900833, established in DRIENERLOLAAN 5, ENSCHEDE 7522 NB, Netherlands,

18. **UNIVERSIDAD POLITECNICA DE MADRID (UPM)**, PIC 999974844, established in CALLE RAMIRO DE MAEZTU 7 EDIFICIO RECTORADO, MADRID 28040, Spain,

19. **ACADEMISCH ZIEKENHUIS GRONINGEN (UMCG)**, PIC 999914801, established in HANZEPLEIN 1, GRONINGEN 9713 GZ, Netherlands,

20. **STICHTING AMSTERDAM UMC (AUMC)**, PIC 919322739, established in DE BOELELAAN 1117, AMSTERDAM 1081 HV, Netherlands,

21. **UNIVERSITEIT MAASTRICHT (UM)**, PIC 999975911, established in MINDERBROEDERSBERG 4, MAASTRICHT 6200 MD, Netherlands,

22. **EATRIS ERIC (EATRIS)**, PIC 941506445, established in DE BOELELAAN 1118, AMSTERDAM 1081 HZ, Netherlands,

23. **FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS (FGB)**, PIC 962478330, established in VIA ABATE EUSTASIO 30, VALENZANO BARI 70010, Italy,

24. **ASSISTANCE PUBLIQUE HOPITAUX DE PARIS (APHP)**, PIC 999645432, established in 55 BOULEVARD DIDEROT, PARIS 75012, France,

25. **UNIVERSITEIT HASSELT (UHASSELT)**, PIC 999874934, established in MARTELARENLAAN 42, HASSELT 3500, Belgium,

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26. **EURORDIS - RARE DISEASES EUROPE (EURORDIS)**, PIC 965288323, established in RUE DIDOT 96, Paris 75014, France,

27. **VIESOJI ISTAIGA VILNIAUS UNIVERSITETO LIGONINE SANTAROS KLINIKOS (VULSK)**, PIC 991636530, established in SANTARISKIU G 2, VILNIUS LT-08661, Lithuania,

28. **UNIVERSIDADE DE COIMBRA (UC)**, PIC 997826391, established in PACO DAS ESCOLAS, COIMBRA 3004-531, Portugal,

29. **FONDATION MALADIES RARES (FFRD)**, PIC 954438485, established in RUE DIDOT 96, PARIS 75014, France,

30. **ASS FRANCAISE CONTRE LES MYOPATHIES (AFM)**, PIC 959828387, established in 47-83 47 BOULEVARD DE L'HOPITAL, INSTITUT DE MYOLO, PARIS 75013, France,

31. **BERNU KLINISKA UNIVERSITATES SLIMNICA VALSTS SIA (CCUH)**, PIC 904374748, established in VIENIBAS GATVE 45, RIGA 1004, Latvia,

32. **AICIB - AGENCIA DE INVESTIGACAO CLINICA E INOVACAO BIOMEDICA (AICIB)**, PIC 892687606, established in RUA DE SANTA CATARINA 1288, PORTO 4000-447, Portugal,

33. **INSTITUT ZA MOLEKULARNU GENETIKU I GENETICKO INZENJERSTVO (IMGGE)**, PIC 986427921, established in VOJVODE STEPE 444A, BEOGRAD 11010, Serbia,

34. **RARE DISEASES INTERNATIONAL (RDI)**, PIC 881348694, established in 96 RUE DIDOT, PARIS 75014, France,

35. **ACIBADEM MEHMET ALI AYDINLAR UNIVERSITY (ACU)**, PIC 959704421, established in ICERENKOY MAH. KAYISDAGI CAD. NO/32 ATASEHIR, ISTANBUL 34752, Türkiye,

36. **AIT AUSTRIAN INSTITUTE OF TECHNOLOGY GMBH (AIT)**, PIC 999584128, established in GIEFINGGASSE 4, WIEN 1210, Austria,

37. **UNIVERSITE D'AIX MARSEILLE (AMU)**, PIC 955518483, established in BOULEVARD CHARLES LIVON 58 LE PHARO, MARSEILLE 13284, France,

38. **AZIENDA OSPEDALIERA UNIVERSITARIA MEYER IRCCS (AOU Meyer IRCCS)**, PIC 998778543, established in VIALE PIERACCINI 24, FIRENZE 50139, Italy,

39. **AZIENDA SANITARIA UNIVERSITARIA FRIULI CENTRALE (ASU-FC)**, PIC 894464355, established in VIA POZZUOLO 330, UDINE 33100, Italy,

40. **BAR ILAN UNIVERSITY (BIU)**, PIC 999886574, established in BAR ILAN UNIVERSITY CAMPUS, RAMAT GAN 52900, Israel,

41. **BUNDESMINISTERIUM FUER BILDUNG UND FORSCHUNG (BMBF)**, PIC 999835455, established in Heinemannstrasse 2, BONN 53175, Germany,

42. **ST. ANNA KINDERKREBSFORSCHUNG GMBH (CCRI GmbH)**, PIC 891384896, established in ZIMMERMANNPLATZ 10, WIEN 1090, Austria,

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43. **CENTOGENE GMBH (CENTOGENE)**, PIC 878333449, established in AM.STRANDE 7, ROSTOCK 18055, Germany,

44. **CHARITE - UNIVERSITAETSMEDIZIN BERLIN (CHARITE)**, PIC 999992692, established in Chariteplatz 1, BERLIN 10117, Germany,

45. **CHECKIMMUNE GMBH (CHI)**, PIC 889852781, established in CAMPUS VIRCHOW KLINIKUM, CRANACH HAUS AUGUSTENBURG PLATZ 1, BERLIN 13353, Germany,

46. **CENTRE HOSPITALIER REG UNIVERSITAIRE DIJON (CHU Dijon)**, PIC 959994451, established in BOULEVARD MAL DE LATTRE DE TASSIGNY 2, DIJON 21000, France,

47. **COPENHAGEN ECONOMICS AS (CE)**, PIC 938801309, established in LANGEBROGADE 1B, KOBENHAVN K 1411, Denmark,

48. **REGION HOVEDSTADEN (REGIONH)**, PIC 999654744, established in KONGENS VAENGE 2, HILLEROD 3400, Denmark,

49. **MINISTRY OF HEALTH (CSO-MOH)**, PIC 999596156, established in YIRMIYAHU 39, JERUSALEM 9101002, Israel,

50. **CONSORZIO PER VALUTAZIONI BIOLOGICHE E FARMACOLOGICHE (CVBF)**, PIC 999717018, established in VIA NICOLO PUTIGNANI 178, BARI 70122, Italy,

51. **STICHTING DUCHENNE DATA FOUNDATION (DDF)**, PIC 899914882, established in WARMOESDREEF 10, BERGEN OP ZOOM 4614 HC, Netherlands,

52. **ELSEVIER BV (ELS)**, PIC 999937014, established in RADARWEG 29, AMSTERDAM 1043NX, Netherlands,

53. **ERASMUS UNIVERSITAIR MEDISCH CENTRUM ROTTERDAM (Erasmus MC)**, PIC 999988424, established in DR MOLEWATERPLEIN 40, ROTTERDAM 3015 GD, Netherlands,

54. **FONDS DE LA RECHERCHE SCIENTIFIQUE- FNRS (F.R.S.-FNRS)**, PIC 999540381, established in RUE D'EGMONT 5, BRUXELLES 1000, Belgium,

55. **FRAUNHOFER GESELLSCHAFT ZUR FORDERUNG DER ANGEWANDTEN FORSCHUNG EV (FHG)**, PIC 999984059, established in HANSASTRASSE 27C, MUNCHEN 80686, Germany,

56. **FONDAZIONE REGIONALE PER LA RICERCA BIOMEDICA (FRRB)**, PIC 929009450, established in PIAZZA CITTA DI LOMBARDIA 1, MILANO 20124, Italy,

57. **ECRIN EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK (ECRIN)**, PIC 948646712, established in 30 BD SAINT-JACQUES BATIMENT B, PARIS 75014, France,

58. **FONDS ZUR FÖRDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG (FWF)**, PIC 998735960, established in GEORG-COCH-PLATZ 2, WIEN 1010, Austria,

59. **INNOVATIONSFONDEN (IFD)**, PIC 939076692, established in OSTERGADE 26 A, KOBENHAVN K 1100, Denmark,

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60. **FUNDACIO PRIVADA PER A LA RECERCA I LA DOCENCIA SANT JOAN DE DEU (FSJD-CERCA)**, PIC 999565601, established in SANTA ROSA 39-4, ESPLUGUES DE LLOBREGAT 08950, Spain,

61. **FUNDACAO PARA A CIENCIA E A TECNOLOGIA (FCT)**, PIC 999543970, established in AVENIDA D CARLOS I 126, LISBOA 1249 074, Portugal,

62. **MINISTERSTVO ZDRAVOTNICTVI CESKE REPUBLIKY (MZd)**, PIC 924144512, established in PALACKEHO NAMESTI 375/4, PRAHA 12801, Czechia,

63. **ASSOCIATION GENETHON (GNT)**, PIC 998217883, established in RUE DE L INTERNATIONALE 1 BIS, EVRY 91002, France,

64. **GEORGIAN FOUNDATION FOR GENETIC AND RARE DISEASES (GERAD)**, PIC 953089312, established in TARKHNISHVILI STREET 9 APT 5, TBIILISI 0179, Georgia,

65. **REGION STOCKHOLM (RS)**, PIC 999522921, established in HANTVERKARGATAN 45, STOCKHOLM 104 22, Sweden,

66. **JOHANN WOLFGANG GOETHE-UNIVERSITAET FRANKFURT AM MAIN (GUF)**, PIC 999978724, established in THEODOR W ADORNO PLATZ 1, FRANKFURT AM MAIN 60629, Germany,

67. **THE HEALTH RESEARCH BOARD (HRB)**, PIC 999546686, established in 67 72 LOWER MOUNT STREET, DUBLIN D02 H638, Ireland,

68. **IZMIR BIYOTIP VE GENOM MERKEZI (İBG)**, PIC 906758620, established in MITHATPASA CAD. NO:58/5 BALCOVA, IZMIR 35340, Türkiye,

69. **RANNSOKNAMIDSTOD ISLANDS (Rannis)**, PIC 999547268, established in BORGARTUNI 30, REYKJAVIK 105, Iceland,

70. **IMAGINE INSTITUT DES MALADIES GENETIQUES NECKER ENFANTS MALADES FONDATION (IMAGINE)**, PIC 955276177, established in 24 BD DU MONTPARNASSE, PARIS 15 75015, France,

71. **INSTYTUT GENETYKI CZLOWIEKA POLSKIEJ AKADEMII NAUK (IGC PAN)**, PIC 982958425, established in STRZESZYNSKA 32, POZNAN 60-479, Poland,

72. **INSTITUTO DE SALUD CARLOS III (ISCIII)**, PIC 999507886, established in MONFORTE DE LEMOS 5, MADRID 28029, Spain,

73. **INSTITUTO NACIONAL DE SAUDE DR. RICARDO JORGE (INSA)**, PIC 998308190, established in AVENIDA PADRE CRUZ, LISBOA 1649-016, Portugal,

74. **ISTITUTO ORTOPEDICO RIZZOLI (IOR)**, PIC 999445709, established in VIA DI BARBIANO 1/10, BOLOGNA 40136, Italy,

75. **ISTITUTO SUPERIORE DI SANITA (ISS)**, PIC 999978821, established in Viale Regina Elena 299, ROMA 00161, Italy,

76. **MINISTERO DELLA SALUTE (IT-MOH)**, PIC 999531942, established in Via Giorgio Ribotta 5, ROMA 00144, Italy,

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77. **KATHOLIEKE UNIVERSITEIT LEUVEN (KU Leuven)**, PIC 999991334, established in OUDE MARKT 13, LEUVEN 3000, Belgium,

78. **LATVIJAS ZINATNES PADOME (LZP)**, PIC 999546589, established in SMILSU IELA 8, RIGA LV-1050, Latvia,

79. **MAPI RESEARCH TRUST (MRT)**, PIC 925695542, established in 27 RUE DE LA VILLETTE, LYON 69003, France,

80. **MEDICAL UNIVERSITY SOFIA (MUS)**, PIC 999857571, established in ACAD IV EVSTATIEV GESHOV ST 15, SOFIA 1431, Bulgaria,

81. **FAKULTNI NEMOCNICE V MOTOLE (MUH)**, PIC 964458391, established in V UVALU 84, PRAHA 5 150 06, Czechia,

82. **Ministero dell'università e della ricerca (MUR)**, PIC 894763406, established in Via Michele Carcani 61, Roma 00153, Italy,

83. **NARODOWE CENTRUM BADAN I ROZWOJU (NCBR)**, PIC 999519720, established in UL. CHMIELNA 69, WARSZAWA 00-801, Poland,

84. **ETHNIKO KAI KAPODISTRIAKO PANEPISTIMIO ATHINON (NKUA)**, PIC 999643007, established in 6 CHRISTOU LADA STR, ATHINA 10561, Greece,

85. **MINISTERSTVO ZDRAVOTNICTVA SLOVENSKEJ REPUBLIKY (MoH SR)**, PIC 999825173, established in LIMBOVA 2, BRATISLAVA 83752, Slovakia,

86. **ENOSI SPANION ASTHENON ELLADOS (RDG)**, PIC 883276763, established in KAPNIKAREAS 19A, ATHINA 105 56, Greece,

87. **REGION SYDDANMARK (REGIONSYD)**, PIC 999602073, established in DAMHAVEN 12, VEJLE 7100, Denmark,

88. **OSPEDALE PEDIATRICO BAMBINO GESU (OPBG)**, PIC 998837810, established in PIAZZA SANT ONOFRIO 4, ROMA 00165, Italy,

89. **OSPEDALE SAN RAFFAELE SRL (OSR)**, PIC 953176030, established in VIA OLGETTINA 60, MILANO 20132, Italy,

90. **INSTITUT JOZEF STEFAN (JSI)**, PIC 999971837, established in Jamova 39, LJUBLJANA 1000, Slovenia,

91. **NORGES FORSKNINGSRAD (RCN)**, PIC 999460453, established in DRAMMENSVEIEN 288, OSLO 0283, Norway,

92. **FONDS VOOR WETENSCHAPPELIJK ONDERZOEK-VLAANDEREN (FWO)**, PIC 997949484, established in LEUVENSEWEG 38, BRUSSEL 1000, Belgium,

93. **RIGAS AUSTRUMU KLINISKA UNIVERSITATES SLIMNICA SIA (REUH)**, PIC 973366483, established in HIPOKRATA IELA 2, RIGA LV-1079, Latvia,

94. **IDRYMA EREVNAS KAI KAINOTOMIAS (RIF)**, PIC 999946035, established in ANDREA MICHALAKOPOULOU 29 A, NICOSIA 1075, Cyprus,

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95. **ROYAL COLLEGE OF SURGEONS IN IRELAND (RCSI)**, PIC 999867368, established in ST STEPHEN'S GREEN 123, DUBLIN 2, Ireland,

96. **RIGAS STRADINA UNIVERSITATE (RSU)**, PIC 999843118, established in Dzirciema street 16, RIGA 1007, Latvia,

97. **SCIENSANO (Sciensano)**, PIC 906160809, established in JULIETTE WYTSMANSTRAAT 14, ELSENE 1050, Belgium,

98. **SERVICE PUBLIC DE WALLONIE (SPW)**, PIC 999811884, established in Place de la Wallonie 1, Namur 5100, Belgium,

99. **SIGMUND FREUD PRIVATUNIVERSITAT WIEN GMBH (SFU)**, PIC 996709824, established in FREUDPLATZ 1, WIEN 1020, Austria,

100. **SIHTASUTUS EESTI TEADUSAGENTUUR (ETAg)**, PIC 998483760, established in SOOLA 8, TARTU 51004, Estonia,

101. **SLOVENSKA AKADEMIA VIED (SAS)**, PIC 999530390, established in STEFANIKOVA 49, BRATISLAVA 814 38, Slovakia,

102. **SONIO (Sonio)**, PIC 886915427, established in 24 RUE DU FAUBOURG SAINT-JACQUES, PARIS 75014, France,

103. **SOTSIAALMINISTEERIUM (MOSAE)**, PIC 998429731, established in Suur-Ameerika 1, TALLINN 10122, Estonia,

104. **VETENSKAPSRADET - SWEDISH RESEARCH COUNCIL (SRC)**, PIC 999586165, established in BOX 1035, STOCKHOLM 101 38, Sweden,

105. **TEDDY - EUROPEAN NETWORK OF EXCELLENCE FOR PAEDIATRIC CLINICAL RESEARCH (TEDDY)**, PIC 910591963, established in VIA LUIGI PORTA 14, PAVIA 231261, Italy,

106. **TEKKARE (TEKKARE)**, PIC 881967069, established in 11-19 RUE DE LA VANNE, SOPARQ, BAT C, MONTROUGE 92120, France,

107. **THALASSAEMIA INTERNATIONAL FEDERATION (TIF)**, PIC 940669626, established in AKROPOLEOS 21 STROVOLOS, LEFKOSIA 2006, Cyprus,

108. **TURKIYE BILIMSEL VE TEKNOLOJIK ARASTIRMA KURUMU (TUBITAK)**, PIC 999587135, established in Ataturk Bulvari 221, ANKARA 06100, Türkiye,

109. **REGIONE TOSCANA (RT (TuscReg))**, PIC 998823842, established in Palazzo Strozzi Sacrati - Piazza del Duomo 10, FIRENZE 50122, Italy,

110. **UNIVERSITAT AUTONOMA DE BARCELONA (UAB)**, PIC 999986484, established in EDIF A CAMPUS DE LA UAB BELLATERRA CERDANYOLA V, CERDANYOLA DEL VALLES 08193, Spain,

111. **UNIVERSITY COLLEGE DUBLIN, NATIONAL UNIVERSITY OF IRELAND, DUBLIN (UCD)**, PIC 999974359, established in BELFIELD, DUBLIN 4, Ireland,

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112. **UNIVERSITA CATTOLICA DEL SACRO CUORE (UCSC)**, PIC 999915771, established in LARGO GEMELLI 1, MILANO 20123, Italy,

113. **ITA-SUOMEN YLIOPISTO (UEF)**, PIC 991207984, established in YLIOPISTONRANTA 8, KUOPIO 70211, Finland,

114. **UNIVERSITAETSKLINIKUM AACHEN (UKA)**, PIC 999897632, established in Pauwelsstrasse 30, AACHEN 52074, Germany,

115. **UNIVERSITAETSKLINIKUM FREIBURG (UKLFR)**, PIC 999881918, established in HUGSTETTER STRASSE 49, FREIBURG 79106, Germany,

116. **UNIVERSITA DEGLI STUDI DELLA CAMPANIA LUIGI VANVITELLI (UNICAMPANIA)**, PIC 999848356, established in VIALE ABRAMO LINCOLN 5, CASERTA 81100, Italy,

117. **PANEPISTIMIO KRITIS (UoC)**, PIC 999588978, established in UNIVERSITY CAMPUS GALLOS, RETHIMNO 74100, Greece,

118. **UNIVERSITEIT GENT (UGENT)**, PIC 999986096, established in SINT PIETERSNIEUWSTRAAT 25, GENT 9000, Belgium,

119. **UNIVERZITETNI KLINICNI CENTER LJUBLJANA (UKCL)**, PIC 999882306, established in ZALOSKA CESTA 002, LJUBLJANA 1000, Slovenia,

120. **STICHTING WORLD DUCHENNE ORGANIZATION (WDO)**, PIC 930321860, established in KONINGINNELAAN 69, VEENENDAAL 3905 GG, Netherlands,

121. **UPPSALA UNIVERSITET (UU)**, PIC 999985029, established in VON KRAEMERS ALLE 4, UPPSALA 751 05, Sweden,

122. **CONECT4CHILDREN STICHTING (c4c-S)**, PIC 881618063, established in NICOLAAS BEETSSTRAAT 216, UTRECHT 3511 HG, Netherlands,

123. **UNIVERSITE CADI AYYAD (CAU)**, PIC 998639930, established in BOULEVARD ABDELKARIM KHATTABI, MARRAKECH 40 000, Morocco,

124. **CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS (CNRS)**, PIC 999997930, established in RUE MICHEL ANGE 3, PARIS 75794, France,

125. **CONSORCIO CENTRO DE INVESTIGACION BIOMEDICA EN RED M.P. (CIBER)**, PIC 997154957, established in CALLE MONFORTE DE LEMOS 5, MADRID 28029, Spain,

126. **UNITATEA EXECUTIVA PENTRU FINANTAREA INVATAMANTULUI SUPERIOR A CERCETARII DEZVOLTARII SI INOVARII (UEFISCDI)**, PIC 972130024, established in STR D I MENDELEEV 21-25, BUCURESTI 010362, Romania,

127. **UNIVERSITA DEGLI STUDI DI ROMA LA SAPIENZA (UNIROMA1)**, PIC 999987745, established in Piazzale Aldo Moro 5, ROMA 00185, Italy,

128. **UNIVERSITEIT ANTWERPEN (UANTWERPEN)**, PIC 999902870, established in PRINSSTRAAT 13, ANTWERPEN 2000, Belgium,

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129. **BULGARIAN NATIONAL SCIENCE FUND (BNSF)**, PIC 984222335, established in BLVD KNYAZ DONDUKOV 2 A, SOFIA 1000, Bulgaria,

130. **REGION NORDJYLLAND (NORTH DENMARK REGION) (Aalborg UH)**, PIC 997381064, established in Niels Bohrs Vej 30, AALBORG 9220, Denmark,

131. **REDKI BOLESTI BULGARIA (RDB)**, PIC 880694720, established in NISHAVA 121, SOFIA 1408, Bulgaria,

132. **BIOBANKS AND BIOMOLECULAR RESOURCES RESEARCH INFRASTRUCTURE CONSORTIUM (BBMRI-ERIC) (BBMRI-ERIC)**, PIC 946597878, established in NEUE STIFTINGTALSTRASSE 2/B/6, GRAZ 8010, Austria,

133. **AARHUS UNIVERSITETSHOSPITAL (AarhusUH)**, PIC 999643880, established in PALLE JUUL-JENSENS BOULEVARD 99, AARHUS 8200, Denmark,

134. **ASSOCIATION INTERNATIONALE DE STANDARDISATION BIOLOGIQUE POUR L'EUROPE(IABS-EU) (IABS-EU)**, PIC 934774936, established in 24 RUE JEAN BALDASSINI, LYON 69393, France,

135. **HEALTH RESEARCH CHARITIES IRELAND COMPANY LIMITED BY GUARANTEE (HRCI)**, PIC 880683274, established in 12 CAMDEN ROW, DUBLIN D08 R9CN, Ireland,

136. **LUDWIG-MAXIMILIANS-UNIVERSITAET MUENCHEN (LMU)**, PIC 999978433, established in GESCHWISTER SCHOLL PLATZ 1, MUNCHEN 80539, Germany,

137. **MYSCIENCEWORK (MSW)**, PIC 898132119, established in 101 RUE DE SEVRES LOT 1674, PARIS 75006, France,

138. **FONDS NATIONAL DE LA RECHERCHE (FNR)**, PIC 998597153, established in 2 AVENUE DE L'UNIVERSITE, ESCH-SUR-ALZETTE 4365, Luxembourg,

139. **NEMZETI KUTATASI FEJLESZTESI ES INNOVACIOS HIVATAL (NKFIH)**, PIC 999578696, established in KETHLY ANNA TER 1, BUDAPEST 1077, Hungary,

140. **BUNDESINSTITUT FUR IMPFSTOFFE UND BIOMEDIZINISCHE ARZNEIMITTEL (PEI)**, PIC 998217301, established in PAUL-EHRLICH-STRASSE 51-59, LANGEN 63225, Germany,

141. **PARIS-LODRON-UNIVERSITAT SALZBURG (PLUS)**, PIC 999868047, established in KAPITELGASSE 4-6, SALZBURG 5020, Austria,

142. **SORBONNE UNIVERSITE (SU)**, PIC 909875521, established in 21 RUE DE L'ECOLE DE MEDECINE, PARIS 75006, France,

143. **UNIVERSITA DEGLI STUDI DI SIENA (UNISI)**, PIC 999898020, established in VIA BANCHI DI SOTTO 55, SIENA 53100, Italy,

144. **VERKET FOR INNOVATIONSSYSTEM (Vinnova)**, PIC 999618757, established in MASTER SAMUELSG 56, STOCKHOLM 10158, Sweden,

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145. **FUNDACIO CENTRE DE REGULACIO GENOMICA (CRG-CERCA)**, PIC 999544455, established in CARRER DOCTOR AIGUADER 88, BARCELONA 08003, Spain,

146. **REGION SKANE (GMS-RS)**, PIC 998165794, established in REGION SKANE, KRISTIANSTAD 291 89, Sweden,

147. **VIB VZW (VIB)**, PIC 999651931, established in SUZANNE TASSIERSTRAAT 1, ZWIJNAARDE - GENT 9052, Belgium,

148. **INSTITUT DE PATHOLOGIE ET DE GENETIQUE ASBL (IPG)**, PIC 878266034, established in Av. Georges Lemaitre 25, GOSSELIES 6041, Belgium,

149. **UNIVERSITY OF OTAGO (UO)**, PIC 998331567, established in SAINT DAVID STREET, DUNEDIN 9054, New Zealand,

150. **HOSPITAL SANT JOAN DE DEU (HSJD)**, PIC 997929890, established in PASEO SANT JOAN DE DEU 2, ESPLUGUES DE LLOBREGAT 08950, Spain,

Unless otherwise specified, references to ‘beneficiary’ or ‘beneficiaries’ include the coordinator and affiliated entities (if any).

If only one beneficiary signs the grant agreement (‘mono-beneficiary grant’), all provisions referring to the ‘coordinator’ or the ‘beneficiaries’ will be considered — mutatis mutandis — as referring to the beneficiary.

The parties referred to above have agreed to enter into the Agreement.

By signing the Agreement and the accession forms, the beneficiaries accept the grant and agree to implement the action under their own responsibility and in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

The Agreement is composed of:

Preamble

Terms and Conditions (including Data Sheet)

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Annex 1 Description of the action[1]

Annex 2 Estimated budget for the action

Annex 2a Additional information on unit costs and contributions (if applicable)

Annex 3 Accession forms (if applicable)[2]

Annex 3a Declaration on joint and several liability of affiliated entities (if applicable)[3]

Annex 4 Model for the financial statements

Annex 5 Specific rules (if applicable)

[1] Template published on Portal Reference Documents.
[2] Template published on Portal Reference Documents.
[3] Template published on Portal Reference Documents.

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TERMS AND CONDITIONS

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DATA SHEET

1. General data

Project summary:

Project summary
The European Rare Diseases Research Alliance (ERDERA) aims to improve the health and well-being of the 30 million people living with a rare disease in Europe, by making Europe a world leader in Rare Disease (RD) research and innovation, to support concrete health benefits to rare disease patients, through better prevention, diagnosis and treatment. This Partnership will deliver a RD ecosystem that builds on the successes of previous programmes by supporting robust patient need-led research, developing new diagnostic methods and pathways, spearheading the digital transformational change connecting the dots between care, patient data and research, while ensuring strong alignment of strategies in RD research across countries and regions. Structuring goal-oriented public-private collaborations targeted at interventions all along the R&D value chain will ensure that the journey from knowledge to patient impact is expedited, thereby optimising EU innovation potential in RD. To support its ambition and missions ERDERA has been designed as a comprehensive and integrated ecosystem of which structure can be compared to an institute encompassing three main parts: (i) funding, (ii) internal (in house) Clinical Research Network that implements research activities targeting clinical trial readiness of RDs and accelerating diagnosis and translation of research discovery into improved patient care, and (iii) related supporting services (Data, Expertise, Education and Training) as well as an acceleration hub that serve external and internal RD community, all supported by all-embracing coordination and strategy and foundational (inter)national alignment.

Keywords:

- Rare diseases
- translational research, diagnostics, therapy development, ATMPs, data, education, patients empowerment, public-private collaboration, federated analysis, regulatory compliance, clinical trials

Project number: 101156595

Project name: EUROPEAN RARE DISEASES RESEARCH ALLIANCE

Project acronym: ERDERA

Call: HORIZON-HLTH-2023-DISEASE-07

Topic: HORIZON-HLTH-2023-DISEASE-07-01

Type of action: HORIZON Programme Cofund Actions

Granting authority: European Health and Digital Executive Agency

Grant managed through EU Funding & Tenders Portal: Yes (eGrants)

Project starting date: fixed date: 1 September 2024

Project end date: 31 August 2031

Project duration: 84 months

Consortium agreement: Yes

2. Participants

List of participants:

N°	Role	Short name	Legal name	Ctry	PIC	Total eligible costs (BEN and AE)	Max grant amount
1	COO	INSERM	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE	FR	999997833	9 032 651.75	4 516 325.88
1.1	AE	CAD	Collecteur Analyseur de Données	FR	880793078	716 000.00	358 000.00
2	BEN	TEAMIT	TEAMIT RESEARCH SL	ES	896104237	1 493 375.00	746 687.50

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N°	Role	Short name	Legal name	Ctry	PIC	Total eligible costs (BEN and AE)	Max grant amount
3	BEN	DLR	DEUTSCHES ZENTRUM FUR LUFT - UND RAUMFAHRT EV	DE	999981731	554 051.25	277 025.63
4	BEN	ANR	AGENCE NATIONALE DE LA RECHERCHE	FR	998711613	13 041 861.75	3 907 279.49
5	BEN	FTELE	FONDAZIONE TELETHON ETS	IT	999448716	3 628 310.00	1 401 160.30
6	BEN	LMT	Lietuvos mokslo taryba	LT	997808446	465 802.25	152 891.05
7	BEN	ZonMw	ZORGONDERZOEK NEDERLAND ZON	NL	999544164	5 940 632.50	1 990 795.26
8	BEN	UT	EBERHARD KARLS UNIVERSITAET TUEBINGEN	DE	999991916	2 942 328.75	1 471 164.38
9	BEN	UTARTU	TARTU ULIKOOL	EE	999895013	450 627.50	225 313.75
10	BEN	CNAG	CONSORCIO PARA LA EXPLOTACION DEL CENTRO NACIONAL DE ANALISIS GENOMICO	ES	882802433	1 962 785.71	981 392.86
11	BEN	SRUMC	STICHTING RADBOUD UNIVERSITAIR MEDISCH CENTRUM	NL	892057785	3 163 050.00	1 581 525.00
12	BEN	TUM	TECHNISCHE UNIVERSITAET MUENCHEN	DE	999977463	683 125.00	341 562.50
13	BEN	UKHD	UNIVERSITATSKLINIKUM HEIDELBERG	DE	999841081	3 181 611.25	1 590 805.63
14	BEN	C-PATH	CRITICAL PATH INSTITUTE STICHTING	NL	887895418	924 601.25	462 300.63
15	BEN	VHIR	FUNDACIO HOSPITAL UNIVERSITARI VALL D'HEBRON - INSTITUT DE RECERCA	ES	999541642	1 543 050.00	771 525.00
16	BEN	LUMC	ACADEMISCH ZIEKENHUIS LEIDEN	NL	999990849	1 297 155.00	648 577.50
17	BEN	UTWENTE	UNIVERSITEIT TWENTE	NL	999900833	377 120.00	188 560.00
18	BEN	UPM	UNIVERSIDAD POLITECNICA DE MADRID	ES	999974844	1 076 878.75	538 439.38
19	BEN	UMCG	ACADEMISCH ZIEKENHUIS GRONINGEN	NL	999914801	1 593 566.25	796 783.13
20	BEN	AUMC	STICHTING AMSTERDAM UMC	NL	919322739	668 798.75	334 399.38
21	BEN	UM	UNIVERSITEIT MAASTRICHT	NL	999975911	367 325.00	183 662.50
22	BEN	EATRIS	EATRIS ERIC	NL	941506445	1 016 710.00	508 355.00
23	BEN	FGB	FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS	IT	962478330	798 285.00	399 142.50
24	BEN	APHP	ASSISTANCE PUBLIQUE HOPITAUX DE PARIS	FR	999645432	1 616 832.50	808 416.25
25	BEN	UHASSELT	UNIVERSITEIT HASSELT	BE	999874934	294 187.50	147 093.75
26	BEN	EURORDIS	EURORDIS - RARE DISEASES EUROPE	FR	965288323	1 622 066.25	811 033.13
27	BEN	VULSK	VIESOJI ISTAIGA VILNIAUS UNIVERSITETO LIGONINE SANTAROS KLINIKOS	LT	991636530	732 225.00	366 112.50
28	BEN	UC	UNIVERSIDADE DE COIMBRA	PT	997826391	758 030.00	379 015.00
29	BEN	FFRD	FONDATION MALADIES RARES	FR	954438485	1 966 776.25	983 388.13
30	BEN	AFM	ASS FRANCAISE CONTRE LES MYOPATHIES	FR	959828387	364 500.00	182 250.00
31	BEN	CCUH	BERNU KLINISKA UNIVERSITATES SLIMNICA VALSTS SIA	LV	904374748	235 605.00	117 802.50
32	BEN	AICIB	AICIB - AGENCIA DE INVESTIGACAO CLINICA E INOVACAO BIOMEDICA	PT	892687606	160 420.00	80 210.00
33	BEN	IMGGE	INSTITUT ZA MOLEKULARNU GENETIKU I GENETICKO INZENJERSTVO	RS	986427921	56 447.50	28 223.75
34	BEN	RDI	RARE DISEASES INTERNATIONAL	FR	881348694	222 375.00	111 187.50
35	BEN	ACU	ACIBADEM MEHMET ALI AYDINLAR UNIVERSITY	TR	959704421	17 946.25	8 973.13
36	BEN	AIT	AIT AUSTRIAN INSTITUTE OF TECHNOLOGY GMBH	AT	999584128	282 503.75	141 251.88
37	BEN	AMU	UNIVERSITE D'AIX MARSEILLE	FR	955518483	221 450.00	110 725.00
38	BEN	AOU Meyer IRCCS	AZIENDA OSPEDALIERA UNIVERSITARIA MEYER IRCCS	IT	998778543	76 875.00	38 437.50
39	BEN	ASU-FC	AZIENDA SANITARIA UNIVERSITARIA FRIULI CENTRALE	IT	894464355	330 225.00	165 112.50
40	BEN	BIU	BAR ILAN UNIVERSITY	IL	999886574	99 617.50	49 808.75

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N°	Role	Short name	Legal name	Ctry	PIC	Total eligible costs (BEN and AE)	Max grant amount
41	BEN	BMBF	BUNDESMINISTERIUM FUER BILDUNG UND FORSCHUNG	DE	999835455	9 008 750.00	2 683 005.99
42	BEN	CCRI GmbH	ST. ANNA KINDERKREBSFORSCHUNG GMBH	AT	891384896	307 350.00	153 675.00
43	BEN	CENTOGENE	CENTOGENE GMBH	DE	878333449	150 000.00	75 000.00
44	BEN	CHARITE	CHARITE - UNIVERSITAETSMEDIZIN BERLIN	DE	999992692	656 251.25	328 125.63
45	BEN	CHI	CHECKIMMUNE GMBH	DE	889852781	262 998.75	131 499.38
46	BEN	CHU Dijon	CENTRE HOSPITALIER REG UNIVERSITAIRE DIJON	FR	959994451	223 125.00	111 562.50
47	BEN	CE	COPENHAGEN ECONOMICS AS	DK	938801309	506 967.50	253 483.75
48	BEN	REGIONH	REGION HOVEDSTADEN	DK	999654744	150 000.00	75 000.00
49	BEN	CSO-MOH	MINISTRY OF HEALTH	IL	999596156	1 145 100.00	434 008.01
50	BEN	CVBF	CONSORZIO PER VALUTAZIONI BIOLOGICHE E FARMACOLOGICHE	IT	999717018	277 275.00	138 637.50
51	BEN	DDF	STICHTING DUCHENNE DATA FOUNDATION	NL	899914882	284 825.00	142 412.50
52	BEN	ELS	ELSEVIER BV	NL	999937014	421 200.00	210 600.00
53	BEN	Erasmus MC	ERASMUS UNIVERSITAIR MEDISCH CENTRUM ROTTERDAM	NL	999988424	817 978.75	408 989.38
54	BEN	F.R.S.-FNRS	FONDS DE LA RECHERCHE SCIENTIFIQUE- FNRS	BE	999540381	934 575.00	283 821.89
55	BEN	FHG	FRAUNHOFER GESELLSCHAFT ZUR FORDERUNG DER ANGEWANDTEN FORSCHUNG EV	DE	999984059	765 065.63	382 532.82
56	BEN	FRRB	FONDAZIONE REGIONALE PER LA RICERCA BIOMEDICA	IT	929009450	4 532 575.00	1 282 839.44
57	BEN	ECRIN	ECRIN EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK	FR	948646712	57 850.00	28 925.00
58	BEN	FWF	FONDS ZUR FÖRDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG	AT	998735960	2 747 575.00	794 930.67
59	BEN	IFD	INNOVATIONSFONDEN	DK	939076692	3 031 475.00	864 008.80
60	BEN	FSJD-CERCA	FUNDACIO PRIVADA PER A LA RECERCA I LA DOCENCIA SANT JOAN DE DEU	ES	999565601	201 382.50	100 691.25
61	BEN	FCT	FUNDACAO PARA A CIENCIA E A TECNOLOGIA	PT	999543970	1 073 950.00	316 043.45
62	BEN	MZd	MINISTERSTVO ZDRAVOTNICTVI CESKE REPUBLIKY	CZ	924144512	1 505 000.00	439 620.90
62.1	AE	AZV	AGENTURA PRO ZDRAVOTNICKY VYZKUM CESKE REPUBLIKY AZV CR	CZ	878890229	16 422.50	8 211.25
63	BEN	GNT	ASSOCIATION GENETHON	FR	998217883	897 927.50	448 963.75
64	BEN	GERAD	GEORGIAN FOUNDATION FOR GENETIC AND RARE DISEASES	GE	953089312	40 718.75	20 359.38
65	BEN	RS	REGION STOCKHOLM	SE	999522921	37 875.00	18 937.50
66	BEN	GUF	JOHANN WOLFGANG GOETHE-UNIVERSITAET FRANKFURT AM MAIN	DE	999978724	82 976.25	41 488.13
67	BEN	HRB	THE HEALTH RESEARCH BOARD	IE	999546686	1 699 415.00	597 314.15
68	BEN	İBG	IZMIR BIYOTIP VE GENOM MERKEZI	TR	906758620	444 621.25	222 310.63
69	BEN	Rannis	RANNSOKNAMIDSTOD ISLANDS	IS	999547268	463 146.00	150 500.42
70	BEN	IMAGINE	IMAGINE INSTITUT DES MALADIES GENETIQUES NECKER ENFANTS MALADES FONDATION	FR	955276177	472 423.50	236 211.75
71	BEN	IGC PAN	INSTYTUT GENETYKI CZLOWIEKA POLSKIEJ AKADEMII NAUK	PL	982958425	52 500.00	26 250.00
72	BEN	ISCIII	INSTITUTO DE SALUD CARLOS III	ES	999507886	5 425 418.75	1 899 967.27
73	BEN	INSA	INSTITUTO NACIONAL DE SAUDE DR. RICARDO JORGE	PT	998308190	88 560.00	44 280.00
74	BEN	IOR	ISTITUTO ORTOPEDICO RIZZOLI	IT	999445709	32 500.00	16 250.00

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N°	Role	Short name	Legal name	Ctry	PIC	Total eligible costs (BEN and AE)	Max grant amount
75	BEN	ISS	ISTITUTO SUPERIORE DI SANITA	IT	999978821	148 062.50	74 031.25
76	BEN	IT-MOH	MINISTERO DELLA SALUTE	IT	999531942	3 033 325.00	865 673.80
77	BEN	KU Leuven	KATHOLIEKE UNIVERSITEIT LEUVEN	BE	999991334	535 041.25	267 520.63
78	BEN	LZP	LATVIJAS ZINATNES PADOME	LV	999546589	322 075.00	103 435.63
79	BEN	MRT	MAPI RESEARCH TRUST	FR	925695542	276 700.00	138 350.00
80	BEN	MUS	MEDICAL UNIVERSITY SOFIA	BG	999857571	52 500.00	26 250.00
81	BEN	MUH	FAKULTNI NEMOCNICE V MOTOLE	CZ	964458391	313 600.00	156 800.00
82	BEN	MUR	Ministero dell'università e della ricerca	IT	894763406	3 028 325.00	861 173.80
83	BEN	NCBR	NARODOWE CENTRUM BADAN I ROZWOJU	PL	999519720	3 625 825.00	1 026 060.06
84	BEN	NKUA	ETHNIKO KAI KAPODISTRIAKO PANEPISTIMIO ATHINON	EL	999643007	52 500.00	26 250.00
85	BEN	MoH SR	MINISTERSTVO ZDRAVOTNICTVA SLOVENSKEJ REPUBLIKY	SK	999825173	112 350.00	56 175.00
86	BEN	RDG	ENOSI SPANION ASTHENON ELLADOS	EL	883276763	79 850.00	39 925.00
87	BEN	REGIONSYD	REGION SYDDANMARK	DK	999602073	150 000.00	75 000.00
88	BEN	OPBG	OSPEDALE PEDIATRICO BAMBINO GESU	IT	998837810	174 375.00	87 187.50
89	BEN	OSR	OSPEDALE SAN RAFFAELE SRL	IT	953176030	628 577.50	314 288.75
90	BEN	JSI	INSTITUT JOZEF STEFAN	SI	999971837	77 850.00	38 925.00
91	BEN	RCN	NORGES FORSKNINGSRAD	NO	999460453	1 581 182.00	464 271.41
92	BEN	FWO	FONDS VOOR WETENSCHAPPELIJK ONDERZOEK-VLAANDEREN	BE	997949484	2 139 575.00	620 594.41
93	BEN	REUH	RIGAS AUSTRUMU KLINISKA UNIVERSITATES SLIMNICA SIA	LV	973366483	189 825.00	94 912.50
94	BEN	RIF	IDRYMA EREVNAS KAI KAINOTOMIAS	CY	999946035	3 038 457.50	870 292.51
95	BEN	RCSI	ROYAL COLLEGE OF SURGEONS IN IRELAND	IE	999867368	76 875.00	38 437.50
96	BEN	RSU	RIGAS STRADINA UNIVERSITATE	LV	999843118	30 860.00	15 430.00
97	BEN	Sciensano	SCIENSANO	BE	906160809	406 875.00	203 437.50
98	BEN	SPW	SERVICE PUBLIC DE WALLONIE	BE	999811884	3 039 575.00	871 298.80
99	BEN	SFU	SIGMUND FREUD PRIVATUNIVERSITAT WIEN GMBH	AT	996709824	276 387.50	138 193.75
100	BEN	ETAg	SIHTASUTUS EESTI TEADUSAGENTUUR	EE	998483760	170 825.00	60 526.56
101	BEN	SAS	SLOVENSKA AKADEMIA VIED	SK	999530390	140 825.00	52 169.75
102	BEN	Sonio	SONIO	FR	886915427	226 075.00	113 037.50
103	BEN	MOSAE	SOTSIAALMINISTEERIUM	EE	998429731	171 325.00	60 976.56
104	BEN	SRC	VETENSKAPSRADET - SWEDISH RESEARCH COUNCIL	SE	999586165	1 491 983.00	437 258.38
105	BEN	TEDDY	TEDDY - EUROPEAN NETWORK OF EXCELLENCE FOR PAEDIATRIC CLINICAL RESEARCH	IT	910591963	71 800.00	35 900.00
106	BEN	TEKKARE	TEKKARE	FR	881967069	540 000.00	270 000.00
107	BEN	TIF	THALASSAEMIA INTERNATIONAL FEDERATION	CY	940669626	74 850.00	37 425.00
108	BEN	TUBITAK	TURKIYE BILIMSEL VE TEKNOLOJIK ARASTIRMA KURUMU	TR	999587135	1 545 275.00	458 588.15
109	BEN	RT (TuscReg)	REGIONE TOSCANA	IT	998823842	932 217.50	281 700.20
110	BEN	UAB	UNIVERSITAT AUTONOMA DE BARCELONA	ES	999986484	189 805.00	94 902.50
111	BEN	UCD	UNIVERSITY COLLEGE DUBLIN, NATIONAL UNIVERSITY OF IRELAND, DUBLIN	IE	999974359	58 130.00	29 065.00
112	BEN	UCSC	UNIVERSITA CATTOLICA DEL SACRO CUORE	IT	999915771	162 463.75	81 231.88
113	BEN	UEF	ITA-SUOMEN YLIOPISTO	FI	991207984	287 760.00	143 880.00

N°	Role	Short name	Legal name	Ctry	PIC	Total eligible costs (BEN and AE)	Max grant amount
114	BEN	UKA	UNIVERSITAETSKLINIKUM AACHEN	DE	999897632	128 062.50	64 031.25
115	BEN	UKLFR	UNIVERSITAETSKLINIKUM FREIBURG	DE	999881918	400 923.75	200 461.88
116	BEN	UNICAMPANIA	UNIVERSITA DEGLI STUDI DELLA CAMPANIA LUIGI VANVITELLI	IT	999848356	76 875.00	38 437.50
117	BEN	UoC	PANEPISTIMIO KRITIS	EL	999588978	52 500.00	26 250.00
118	BEN	UGENT	UNIVERSITEIT GENT	BE	999986096	198 750.00	99 375.00
119	BEN	UKCL	UNIVERZITETNI KLINICNI CENTER LJUBLJANA	SI	999882306	76 875.00	38 437.50
120	BEN	WDO	STICHTING WORLD DUCHENNE ORGANIZATION	NL	930321860	193 078.75	96 539.38
121	BEN	UU	UPPSALA UNIVERSITET	SE	999985029	493 887.50	246 943.75
122	BEN	c4c-S	CONECT4CHILDREN STICHTING	NL	881618063	106 621.25	53 310.63
123	BEN	CAU	UNIVERSITE CADI AYYAD	MA	998639930	68 993.75	34 496.88
124	BEN	CNRS	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS	FR	999997930	212 352.50	106 176.25
125	BEN	CIBER	CONSORCIO CENTRO DE INVESTIGACION BIOMEDICA EN RED M.P.	ES	997154957	325 196.25	162 598.13
126	BEN	UEFISCDI	UNITATEA EXECUTIVA PENTRU FINANTAREA INVATAMANTULUI SUPERIOR A CERCETARII DEZVOLTARII SI INOVARII	RO	972130024	3 031 775.00	864 278.80
127	BEN	UNIROMA1	UNIVERSITA DEGLI STUDI DI ROMA LA SAPIENZA	IT	999987745	85 178.75	42 589.38
128	BEN	UANTWERPEN	UNIVERSITEIT ANTWERPEN	BE	999902870	51 250.00	25 625.00
129	BEN	BNSF	BULGARIAN NATIONAL SCIENCE FUND	BG	984222335	253 325.00	88 168.60
130	BEN	Aalborg UH	REGION NORDJYLLAND (NORTH DENMARK REGION)	DK	997381064	52 500.00	26 250.00
131	BEN	RDB	REDKI BOLESTI BULGARIA	BG	880694720	32 325.00	16 162.50
132	BEN	BBMRI-ERIC	BIOBANKS AND BIOMOLECULAR RESOURCES RESEARCH INFRASTRUCTURE CONSORTIUM (BBMRI-ERIC)	AT	946597878	111 878.75	55 939.38
133	BEN	AarhusUH	AARHUS UNIVERSITETSHOSPITAL	DK	999643880	76 875.00	38 437.50
134	BEN	IABS-EU	ASSOCIATION INTERNATIONALE DE STANDARDISATION BIOLOGIQUE POUR L'EUROPE(IABS-EU)	FR	934774936	98 812.50	49 406.25
135	BEN	HRCI	HEALTH RESEARCH CHARITIES IRELAND COMPANY LIMITED BY GUARANTEE	IE	880683274	47 625.00	23 812.50
136	BEN	LMU	LUDWIG-MAXIMILIANS-UNIVERSITAET MUENCHEN	DE	999978433	0.00	0.00
136.1	AE	KUM	KLINIKUM DER UNIVERSITAT MUNCHEN	DE	995625946	631 666.25	315 833.13
137	BEN	MSW	MYSCIENCEWORK	FR	898132119	315 000.00	157 500.00
138	BEN	FNR	FONDS NATIONAL DE LA RECHERCHE	LU	998597153	1 029 315.00	313 158.33
139	BEN	NKFIH	NEMZETI KUTATASI FEJLESZTESI ES INNOVACIOS HIVATAL	HU	999578696	922 075.00	272 571.89
140	BEN	PEI	BUNDESINSTITUT FUR IMPFSTOFFE UND BIOMEDIZINISCHE ARZNEIMITTEL	DE	998217301	257 069.38	128 534.69
141	BEN	PLUS	PARIS-LODRON-UNIVERSITAT SALZBURG	AT	999868047	317 472.50	158 736.25
142	BEN	SU	SORBONNE UNIVERSITE	FR	909875521	24 062.50	12 031.25
143	BEN	UNISI	UNIVERSITA DEGLI STUDI DI SIENA	IT	999898020	76 875.00	38 437.50
144	BEN	Vinnova	VERKET FOR INNOVATIONSSYSTEM	SE	999618757	1 447 611.00	425 956.62
145	BEN	CRG-CERCA	FUNDACIO CENTRE DE REGULACIO GENOMICA	ES	999544455	141 750.00	70 875.00
146	BEN	GMS-RS	REGION SKANE	SE	998165794	37 875.00	18 937.50
147	BEN	VIB	VIB VZW	BE	999651931	25 625.00	12 812.50
148	BEN	IPG	INSTITUT DE PATHOLOGIE ET DE GENETIQUE ASBL	BE	878266034	52 500.00	26 250.00
149	BEN	UO	UNIVERSITY OF OTAGO	NZ	998331567	63 600.00	31 800.00

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N°	Role	Short name	Legal name	Ctry	PIC	Total eligible costs (BEN and AE)	Max grant amount
150	BEN	HSJD	HOSPITAL SANT JOAN DE DEU	ES	997929890	65 000.00	32 500.00
151	AP	AZ	ASTRAZENECA AB	SE	999941379	0.00	0.00
152	AP	CHEO-RI	CHILDREN'S HOSPITAL OF EASTERN ONTARIO RESEARCH INSTITUTE INC	CA	907681187	0.00	0.00
153	AP	CIHR	CANADIAN INSTITUTES OF HEALTH RESEARCH	CA	960368386	0.00	0.00
154	AP	DFG	DEUTSCHE FORSCHUNGSGEMEINSCHAFT EV	DE	999547462	0.00	0.00
155	AP	FDB	FUJIFILM DIOSYNTH BIOTECHNOLOGIES UK LIMITED	UK	962770494	0.00	0.00
156	AP	FRQS	FONDS DE RECHERCHE DU QUEBEC - SANTE	CA	963122410	0.00	0.00
157	AP	HIPRA	HIPRA HUMAN HEALTH SL	ES	890821326	0.00	0.00
158	AP	LAB HIPRA	LABORATORIOS HIPRA SA	ES	991274041	0.00	0.00
159	AP	MICYRN	MICYRN	CA	880745451	0.00	0.00
160	AP	Miltenyi	MILTENYI BIOTEC BV & CO KG	DE	897602402	0.00	0.00
161	AP (IO)	Pfizer	PFIZER INC	US	887211374	0.00	0.00
162	AP	RCC	DEPARTMENT OF HEALTH GOVERNMENT OF WESTERN AUSTRALIA	AU	960480421	0.00	0.00
163	AP	REI	REITHERA SRL	IT	998129419	0.00	0.00
164	AP	RJF	LABORATORIO REIG JOFRE SA	ES	951005073	0.00	0.00
165	AP	ROCHE	F. HOFFMANN-LA ROCHE AG	CH	999601782	0.00	0.00
166	AP	SNSF	SCHWEIZERISCHER NATIONALFONDS ZUR FORDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG	CH	999540575	0.00	0.00
167	AP	UCB	UCB BIOPHARMA	BE	937666409	0.00	0.00
168	AP	Fraunhofer UK	FRAUNHOFER UK RESEARCH LIMITED	UK	952487039	0.00	0.00
169	AP	GA UK	GENETIC ALLIANCE UK LTD	UK	999790932	0.00	0.00
170	AP	UNEW	UNIVERSITY OF NEWCASTLE UPON TYNE	UK	999985417	0.00	0.00
171	AP	CUH	Cambridge University Hospitals NHS Foundation Trust	UK	991793961	0.00	0.00
172	AP	ULEIC	UNIVERSITY OF LEICESTER	UK	999985514	0.00	0.00
173	AP	QUB-UK	THE QUEEN'S UNIVERSITY OF BELFAST	UK	999992013	0.00	0.00
174	AP	UCL	UNIVERSITY COLLEGE LONDON	UK	999975620	0.00	0.00
175	AP	UCAM	THE CHANCELLOR MASTERS AND SCHOLARS OF THE UNIVERSITY OF CAMBRIDGE	UK	999977172	0.00	0.00
Total						145 830 619.47	56 317 412.61

Coordinator:

– INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM)

3. Grant

Maximum grant amount, total estimated eligible costs and contributions and funding rate:

Total eligible costs (BEN and AE)	Funding rate (%)	Maximum grant amount (Annex 2)	Maximum grant amount (award decision)
145 830 619.47	50	56 317 412.61	56 317 412.61

Grant form: Budget-based

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Grant mode: Action grant

Budget categories/activity types:

- A. Personnel costs
  - A.1 Employees, A.2 Natural persons under direct contract, A.3 Seconded persons
  - A.4 SME owners and natural person beneficiaries

- B. Subcontracting costs

- C. Purchase costs
  - C.1 Travel and subsistence
  - C.2 Equipment
  - C.3 Other goods, works and services

- D. Other cost categories
  - D.1 Financial support to third parties
  - D.2 Internally invoiced goods and services

- E. Indirect costs

Cost eligibility options:

- In-kind contributions eligible costs

- Parental leave

- Project-based supplementary payments

- Average personnel costs (unit cost according to usual cost accounting practices)

- Limitation for subcontracting

- Travel and subsistence:
  - Travel: Actual costs
  - Accommodation: Actual costs
  - Subsistence: Actual costs

- Equipment: depreciation only

- Costs for providing financial support to third parties (actual cost; max amount for each recipient: EUR 10 000 000.00)

- Indirect cost flat-rate: 25% of the eligible direct costs (categories A-D, except volunteers costs, subcontracting costs, financial support to third parties and exempted specific cost categories, if any)

- VAT: Yes

- Other ineligible costs

Budget flexibility: Yes (no flexibility cap)

4. Reporting, payments and recoveries

4.1 Continuous reporting (art 21)

Deliverables: see Funding & Tenders Portal Continuous Reporting tool

4.2 Periodic reporting and payments

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Reporting and payment schedule (art 21, 22):

Reporting					Payments	
Reporting periods			Type	Deadline	Type	Deadline (time to pay)
RP No	Month from	Month to				
					Initial prefinancing	30 days from entry into force/10 days before starting date – whichever is the latest
1	1	26	Periodic report	60 days after end of reporting period	Interim payment	90 days from receiving periodic report
2	27	44	Periodic report	60 days after end of reporting period	Interim payment	90 days from receiving periodic report
3	45	62	Periodic report	60 days after end of reporting period	Interim payment	90 days from receiving periodic report
4	63	74	Periodic report	60 days after end of reporting period	Interim payment	90 days from receiving periodic report
5	75	84	Periodic report	60 days after end of reporting period	Final payment	90 days from receiving periodic report

Prefinancing payments and guarantees:

Prefinancing payment	
Type	Amount
Prefinancing 1 (initial)	22 526 965.04

Reporting and payment modalities (art 21, 22):

Mutual Insurance Mechanism (MIM): Yes

MIM contribution: 5% of the maximum grant amount (2 815 870.63), retained from the initial prefinancing

Restrictions on distribution of initial prefinancing: The prefinancing may be distributed only if the minimum number of beneficiaries set out in the call condititions (if any) have acceded to the Agreement and only to beneficiaries that have acceded.

Interim payment ceiling (if any): 90% of the maximum grant amount

Exception for revenues: Yes

No-profit rule: Yes

Late payment interest: ECB + 3.5%

Bank account for payments:

FR7610071750000000100507196

Conversion into euros: Double conversion

Reporting language: Language of the Agreement

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4.3 Certificates (art 24):

Certificates on the financial statements (CFS):

Conditions:

Schedule: only at final payment, if threshold is reached

Standard threshold (beneficiary-level):

- financial statement: requested EU contribution to costs ≥ EUR 430 000.00

Special threshold for beneficiaries with a systems and process audit(see Article 24): financial statement: requested EU contribution to costs ≥ EUR 725 000.00

4.4 Recoveries (art 22)

First-line liability for recoveries:

Beneficiary termination: Beneficiary concerned

Final payment: Each beneficiary for their own debt

After final payment: Beneficiary concerned

Joint and several liability for enforced recoveries (in case of non-payment):

Individual financial responsibility: Each beneficiary is liable only for its own debts (and those of its affiliated entities, if any)

Joint and several liability of affiliated entities — n/a

5. Consequences of non-compliance, applicable law & dispute settlement forum

Suspension and termination:

Additional suspension grounds (art 31)

Additional termination grounds (art 32)

Applicable law (art 43):

Standard applicable law regime: EU law + law of Belgium

Dispute settlement forum (art 43):

Standard dispute settlement forum:

EU beneficiaries: EU General Court + EU Court of Justice (on appeal)

Non-EU beneficiaries: Courts of Brussels, Belgium (unless an international agreement provides for the enforceability of EU court judgements)

6. Other

Specific rules (Annex 5): Yes

Standard time-limits after project end:

Confidentiality (for X years after final payment): 5

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Record-keeping (for X years after final payment): 5 (or 3 for grants of not more than EUR 60 000)

Reviews (up to X years after final payment): 2

Audits (up to X years after final payment): 2

Extension of findings from other grants to this grant (no later than X years after final payment): 2

Impact evaluation (up to X years after final payment): 5 (or 3 for grants of not more than EUR 60 000)

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CHAPTER 1 GENERAL

ARTICLE 1 — SUBJECT OF THE AGREEMENT

This Agreement sets out the rights and obligations and terms and conditions applicable to the grant awarded for the implementation of the action set out in Chapter 2.

ARTICLE 2 — DEFINITIONS

For the purpose of this Agreement, the following definitions apply:

Actions — The project which is being funded in the context of this Agreement.

Grant — The grant awarded in the context of this Agreement.

EU grants — Grants awarded by EU institutions, bodies, offices or agencies (including EU executive agencies, EU regulatory agencies, EDA, joint undertakings, etc.).

Participants — Entities participating in the action as beneficiaries, affiliated entities, associated partners, third parties giving in-kind contributions, subcontractors or recipients of financial support to third parties.

Beneficiaries (BEN) — The signatories of this Agreement (either directly or through an accession form).

Affiliated entities (AE) — Entities affiliated to a beneficiary within the meaning of Article 187 of EU Financial Regulation 2018/1046[4] which participate in the action with similar rights and obligations as the beneficiaries (obligation to implement action tasks and right to charge costs and claim contributions).

Associated partners (AP) — Entities which participate in the action, but without the right to charge costs or claim contributions.

Purchases — Contracts for goods, works or services needed to carry out the action (e.g. equipment, consumables and supplies) but which are not part of the action tasks (see Annex 1).

Subcontracting — Contracts for goods, works or services that are part of the action tasks (see Annex 1).

In-kind contributions — In-kind contributions within the meaning of Article 2(36) of EU Financial

[4] For the definition, see Article 187 Regulation (EU, Euratom) 2018/1046 of the European Parliament and of the Council of 18 July 2018 on the financial rules applicable to the general budget of the Union, amending Regulations (EU) No 1296/2013, (EU) No 1301/2013, (EU) No 1303/2013, (EU) No 1304/2013, (EU) No 1309/2013, (EU) No 1316/2013, (EU) No 223/2014, (EU) No 283/2014, and Decision No 541/2014/EU and repealing Regulation (EU, Euratom) No 966/2012 ('EU Financial Regulation') (OJ L 193, 30.7.2018, p. 1): "**affiliated entities** [are]:
(a) entities that form a sole beneficiary [(i.e. where an entity is formed of several entities that satisfy the criteria for being awarded a grant, including where the entity is specifically established for the purpose of implementing an action to be financed by a grant)];
(b) entities that satisfy the eligibility criteria and that do not fall within one of the situations referred to in Article 136(1) and 141(1) and that have a link with the beneficiary, in particular a legal or capital link, which is neither limited to the action nor established for the sole purpose of its implementation".

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Regulation 2018/1046, i.e. non-financial resources made available free of charge by third parties.

Fraud — Fraud within the meaning of Article 3 of EU Directive 2017/1371[5] and Article 1 of the Convention on the protection of the European Communities' financial interests, drawn up by the Council Act of 26 July 1995[6], as well as any other wrongful or criminal deception intended to result in financial or personal gain.

Irregularities — Any type of breach (regulatory or contractual) which could impact the EU financial interests, including irregularities within the meaning of Article 1(2) of EU Regulation 2988/95[7].

Grave professional misconduct — Any type of unacceptable or improper behaviour in exercising one's profession, especially by employees, including grave professional misconduct within the meaning of Article 136(1)(c) of EU Financial Regulation 2018/1046.

Applicable EU, international and national law — Any legal acts or other (binding or non-binding) rules and guidance in the area concerned.

Portal — EU Funding & Tenders Portal; electronic portal and exchange system managed by the European Commission and used by itself and other EU institutions, bodies, offices or agencies for the management of their funding programmes (grants, procurements, prizes, etc.).

CHAPTER 2 ACTION

ARTICLE 3 — ACTION

The grant is awarded for the action **101156595** — **ERDERA** ('action'), as described in Annex 1.

ARTICLE 4 — DURATION AND STARTING DATE

The duration and the starting date of the action are set out in the Data Sheet (see Point 1).

CHAPTER 3 GRANT

ARTICLE 5 — GRANT

5.1 Form of grant

The grant is an action grant[8] which takes the form of a budget-based mixed actual cost grant (i.e. a

[5] Directive (EU) 2017/1371 of the European Parliament and of the Council of 5 July 2017 on the fight against fraud to the Union's financial interests by means of criminal law (OJ L 198, 28.7.2017, p. 29).

[6] OJ C 316, 27.11.1995, p. 48.

[7] Council Regulation (EC, Euratom) No 2988/95 of 18 December 1995 on the protection of the European Communities financial interests (OJ L 312, 23.12.1995, p. 1).

[8] For the definition, see Article 180(2)(a) EU Financial Regulation 2018/1046: '**action grant**' means an EU grant to finance "an action intended to help achieve a Union policy objective".

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grant based on actual costs incurred, but which may also include other forms of funding, such as unit costs or contributions, flat-rate costs or contributions, lump sum costs or contributions or financing not linked to costs).

5.2 Maximum grant amount

The maximum grant amount is set out in the Data Sheet (see Point 3) and in the estimated budget (Annex 2).

5.3 Funding rate

The funding rate for costs is 50% of the action's eligible costs.

Contributions are not subject to any funding rate.

5.4 Estimated budget, budget categories and forms of funding

The estimated budget for the action is set out in Annex 2.

It contains the estimated eligible costs and contributions for the action, broken down by participant and budget category.

Annex 2 also shows the types of costs and contributions (forms of funding)[9] to be used for each budget category.

If unit costs or contributions are used, the details on the calculation will be explained in Annex 2a.

5.5 Budget flexibility

The budget breakdown may be adjusted — without an amendment (see Article 39) — by transfers (between participants and budget categories), as long as this does not imply any substantive or important change to the description of the action in Annex 1.

However:

- changes to the budget category for volunteers (if used) always require an amendment
- changes to budget categories with lump sums costs or contributions (if used; including financing not linked to costs) always require an amendment
- changes to budget categories with higher funding rates or budget ceilings (if used) always require an amendment
- addition of amounts for subcontracts not provided for in Annex 1 either require an amendment or simplified approval in accordance with Article 6.2
- other changes require an amendment or simplified approval, if specifically provided for in Article 6.2
- flexibility caps: not applicable.

[9] See Article 125 EU Financial Regulation 2018/1046.

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ARTICLE 6 — ELIGIBLE AND INELIGIBLE COSTS AND CONTRIBUTIONS

In order to be eligible, costs and contributions must meet the **eligibility** conditions set out in this Article.

6.1 General eligibility conditions

The **general eligibility conditions** are the following:

(a) for actual costs:

(i) they must be actually incurred by the beneficiary

(ii) they must be incurred in the period set out in Article 4 (with the exception of costs relating to the submission of the final periodic report, which may be incurred afterwards; see Article 21)

(iii) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(iv) they must be incurred in connection with the action as described in Annex 1 and necessary for its implementation

(v) they must be identifiable and verifiable, in particular recorded in the beneficiary's accounts in accordance with the accounting standards applicable in the country where the beneficiary is established and with the beneficiary's usual cost accounting practices

(vi) they must comply with the applicable national law on taxes, labour and social security and

(vii) they must be reasonable, justified and must comply with the principle of sound financial management, in particular regarding economy and efficiency

(b) for unit costs or contributions (if any):

(i) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(ii) the units must:

- be actually used or produced by the beneficiary in the period set out in Article 4 (with the exception of units relating to the submission of the final periodic report, which may be used or produced afterwards; see Article 21)

- be necessary for the implementation of the action and

(iii) the number of units must be identifiable and verifiable, in particular supported by records and documentation (see Article 20)

(c) for flat-rate costs or contributions (if any):

(i) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

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(ii) the costs or contributions to which the flat-rate is applied must:

- be eligible
- relate to the period set out in Article 4 (with the exception of costs or contributions relating to the submission of the final periodic report, which may be incurred afterwards; see Article 21)

(d) for lump sum costs or contributions (if any):

(i) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(ii) the work must be properly implemented by the beneficiary in accordance with Annex 1

(iii) the deliverables/outputs must be achieved in the period set out in Article 4 (with the exception of deliverables/outputs relating to the submission of the final periodic report, which may be achieved afterwards; see Article 21)

(e) for unit, flat-rate or lump sum costs or contributions according to usual cost accounting practices (if any):

(i) they must fulfil the general eligibility conditions for the type of cost concerned

(ii) the cost accounting practices must be applied in a consistent manner, based on objective criteria, regardless of the source of funding

(f) for financing not linked to costs (if any): the results must be achieved or the conditions must be fulfilled as described in Annex 1.

In addition, for direct cost categories (e.g. personnel, travel & subsistence, subcontracting and other direct costs) only costs that are directly linked to the action implementation and can therefore be attributed to it directly are eligible. They must not include any indirect costs (i.e. costs that are only indirectly linked to the action, e.g. via cost drivers).

In-kind contributions provided by third parties free of charge may be declared as eligible direct costs by the beneficiaries which use them (under the same conditions as if they were their own, provided that they concern only direct costs and that the third parties and their in-kind contributions are set out in Annex 1 (or approved ex post in the periodic report, if their use does not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants; 'simplified approval procedure').

6.2 Specific eligibility conditions for each budget category

For each budget category, the **specific eligibility conditions** are as follows:

Direct costs

A. Personnel costs

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A.1 Costs for employees (or equivalent) are eligible as personnel costs if they fulfil the general eligibility conditions and are related to personnel working for the beneficiary under an employment contract (or equivalent appointing act) and assigned to the action.

They must be limited to salaries (including net payments during parental leave), social security contributions, taxes and other costs linked to the remuneration, if they arise from national law or the employment contract (or equivalent appointing act) and be calculated on the basis of the costs actually incurred, in accordance with the following method:

{daily rate for the person

multiplied by

number of day-equivalents worked on the action (rounded up or down to the nearest half-day)}.

The daily rate must be calculated as:

{annual personnel costs for the person

divided by

215}.

The number of day-equivalents declared for a person must be identifiable and verifiable (see Article 20).

The actual time spent on parental leave by a person assigned to the action may be deducted from the 215 days indicated in the above formula.

The total number of day-equivalents declared in EU grants, for a person for a year, cannot be higher than 215, minus time spent on parental leave (if any).

For personnel which receives supplementary payments for work in projects (project-based remuneration), the personnel costs must be calculated at a rate which:

- corresponds to the actual remuneration costs paid by the beneficiary for the time worked by the person in the action over the reporting period
- does not exceed the remuneration costs paid by the beneficiary for work in similar projects funded by national schemes (‘national projects reference’)
- is defined based on objective criteria allowing to determine the amount to which the person is entitled

and

- reflects the usual practice of the beneficiary to pay consistently bonuses or supplementary payments for work in projects funded by national schemes.

The national projects reference is the remuneration defined in national law, collective labour agreement or written internal rules of the beneficiary applicable to work in projects funded by national schemes.

If there is no such national law, collective labour agreement or written internal rules or if the project-based remuneration is not based on objective criteria, the national project reference will be the average

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remuneration of the person in the last full calendar year covered by the reporting period, excluding remuneration paid for work in EU actions.

If the beneficiary uses average personnel costs (unit cost according to usual cost accounting practices), the personnel costs must fulfil the general eligibility conditions for such unit costs and the daily rate must be calculated:

- using the actual personnel costs recorded in the beneficiary's accounts and excluding any costs which are ineligible or already included in other budget categories; the actual personnel costs may be adjusted on the basis of budgeted or estimated elements, if they are relevant for calculating the personnel costs, reasonable and correspond to objective and verifiable information

and

- according to usual cost accounting practices which are applied in a consistent manner, based on objective criteria, regardless of the source of funding.

A.2 and **A.3 Costs for natural persons working under a direct contract** other than an employment contract and costs for **seconded persons by a third party against payment** are also eligible as personnel costs, if they are assigned to the action, fulfil the general eligibility conditions and:

(a) work under conditions similar to those of an employee (in particular regarding the way the work is organised, the tasks that are performed and the premises where they are performed) and

(b) the result of the work belongs to the beneficiary (unless agreed otherwise).

They must be calculated on the basis of a rate which corresponds to the costs actually incurred for the direct contract or secondment and must not be significantly different from those for personnel performing similar tasks under an employment contract with the beneficiary.

A.4 The work of **SME owners** for the action (i.e. owners of beneficiaries that are small and medium-sized enterprises[10] not receiving a salary) or **natural person beneficiaries** (i.e. beneficiaries that are natural persons not receiving a salary) may be declared as personnel costs, if they fulfil the general eligibility conditions and are calculated as unit costs in accordance with the method set out in Annex 2a.

B. Subcontracting costs

Subcontracting costs for the action (including related duties, taxes and charges, such as non-deductible or non-refundable value added tax (VAT)) are eligible, if they are calculated on the basis of the costs actually incurred, fulfil the general eligibility conditions and are awarded using the

[10] For the definition, see Commission Recommendation 2003/361/EC: micro, small or medium-sized enterprise (SME) are enterprises

- engaged in an economic activity, irrespective of their legal form (including, in particular, self- employed persons and family businesses engaged in craft or other activities, and partnerships or associations regularly engaged in an economic activity) and

- employing fewer than 250 persons (expressed in 'annual working units' as defined in Article 5 of the Recommendation) and which have an annual turnover not exceeding EUR 50 million, and/or an annual balance sheet total not exceeding EUR 43 million.

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beneficiary's usual purchasing practices — provided these ensure subcontracts with best value for money (or if appropriate the lowest price) and that there is no conflict of interests (see Article 12).

Beneficiaries that are 'contracting authorities/entities' within the meaning of the EU Directives on public procurement must also comply with the applicable national law on public procurement.

Subcontracting may cover only a limited part of the action.

The tasks to be subcontracted and the estimated cost for each subcontract must be set out in Annex 1 and the total estimated costs of subcontracting per beneficiary must be set out in Annex 2 (or may be approved ex post in the periodic report, if the use of subcontracting does not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants; 'simplified approval procedure').

C. Purchase costs

Purchase costs for the action (including related duties, taxes and charges, such as non-deductible or non-refundable value added tax (VAT)) are eligible if they fulfil the general eligibility conditions and are bought using the beneficiary's usual purchasing practices — provided these ensure purchases with best value for money (or if appropriate the lowest price) and that there is no conflict of interests (see Article 12).

Beneficiaries that are 'contracting authorities/entities' within the meaning of the EU Directives on public procurement must also comply with the applicable national law on public procurement.

C.1 Travel and subsistence

Purchases for **travel, accommodation** and **subsistence** must be calculated as follows:

- travel: on the basis of the costs actually incurred and in line with the beneficiary's usual practices on travel
- accommodation: on the basis of the costs actually incurred and in line with the beneficiary's usual practices on travel
- subsistence: on the basis of the costs actually incurred and in line with the beneficiary's usual practices on travel .

C.2 Equipment

Purchases of **equipment, infrastructure or other assets** used for the action must be declared as depreciation costs, calculated on the basis of the costs actually incurred and written off in accordance with international accounting standards and the beneficiary's usual accounting practices.

Only the portion of the costs that corresponds to the rate of actual use for the action during the action duration can be taken into account.

Costs for **renting or leasing** equipment, infrastructure or other assets are also eligible, if they do not exceed the depreciation costs of similar equipment, infrastructure or assets and do not include any financing fees.

C.3 Other goods, works and services

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Purchases of **other goods, works and services** must be calculated on the basis of the costs actually incurred.

Such goods, works and services include, for instance, consumables and supplies, promotion, dissemination, protection of results, translations, publications, certificates and financial guarantees, if required under the Agreement.

D. Other cost categories

D.1 Financial support to third parties

Costs for providing financial support to third parties (in the form of **grants, prizes** or similar forms of support; if any) are eligible, if and as declared eligible in the call conditions, if they fulfil the general eligibility conditions, are calculated on the basis of the costs actually incurred and the support is implemented in accordance with the conditions set out in Annex 1.

These conditions must ensure objective and transparent selection procedures and include at least the following:

(a) for grants (or similar):

(i) the maximum amount of financial support for each third party ('recipient'); this amount may not exceed the amount set out in the Data Sheet (see Point 3) or otherwise agreed with the granting authority

(ii) the criteria for calculating the exact amount of the financial support

(iii) the different types of activity that qualify for financial support, on the basis of a closed list

(iv) the persons or categories of persons that will be supported and

(v) the criteria and procedures for giving financial support

(b) for prizes (or similar):

(i) the eligibility and award criteria

(ii) the amount of the prize and

(iii) the payment arrangements.

This cost will not be taken into account for the indirect cost flat-rate.

D.2 Internally invoiced goods and services

Costs for internally invoiced goods and services directly used for the action may be declared as unit cost according to usual cost accounting practices, if and as declared eligible in the call conditions, if they fulfil the general eligibility conditions for such unit costs and the amount per unit is calculated:

- using the actual costs for the good or service recorded in the beneficiary's accounts, attributed either by direct measurement or on the basis of cost drivers, and excluding any cost which are ineligible or already included in other budget categories; the actual costs may be adjusted

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on the basis of budgeted or estimated elements, if they are relevant for calculating the costs, reasonable and correspond to objective and verifiable information

and

- according to usual cost accounting practices which are applied in a consistent manner, based on objective criteria, regardless of the source of funding.

'Internally invoiced goods and services' means goods or services which are provided within the beneficiary's organisation directly for the action and which the beneficiary values on the basis of its usual cost accounting practices.

This cost will not be taken into account for the indirect cost flat-rate.

Indirect costs

E. Indirect costs

Indirect costs will be reimbursed at the flat-rate of 25% of the eligible direct costs (categories A-D, except volunteers costs, subcontracting costs, financial support to third parties and exempted specific cost categories, if any).

Contributions

Not applicable

6.3 Ineligible costs and contributions

The following costs or contributions are **ineligible**:

(a) costs or contributions that do not comply with the conditions set out above (Article 6.1 and 6.2), in particular:

(i) costs related to return on capital and dividends paid by a beneficiary

(ii) debt and debt service charges

(iii) provisions for future losses or debts

(iv) interest owed

(v) currency exchange losses

(vi) bank costs charged by the beneficiary's bank for transfers from the granting authority

(vii) excessive or reckless expenditure

(viii) deductible or refundable VAT (including VAT paid by public bodies acting as public authority)

(ix) costs incurred or contributions for activities implemented during grant agreement suspension (see Article 31)

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(x) in-kind contributions by third parties: not applicable

(b) costs or contributions declared under other EU grants (or grants awarded by an EU Member State, non-EU country or other body implementing the EU budget), except for the following cases:

(i) Synergy actions: not applicable

(ii) if the action grant is combined with an operating grant[11] running during the same period and the beneficiary can demonstrate that the operating grant does not cover any (direct or indirect) costs of the action grant

(c) costs or contributions for staff of a national (or regional/local) administration, for activities that are part of the administration's normal activities (i.e. not undertaken only because of the grant)

(d) costs or contributions (especially travel and subsistence) for staff or representatives of EU institutions, bodies or agencies

(e) other :

(i) country restrictions for eligible costs: not applicable

(ii) costs or contributions declared specifically ineligible in the call conditions.

6.4 Consequences of non-compliance

If a beneficiary declares costs or contributions that are ineligible, they will be rejected (see Article 27).

This may also lead to other measures described in Chapter 5.

CHAPTER 4 GRANT IMPLEMENTATION

SECTION 1 CONSORTIUM: BENEFICIARIES, AFFILIATED ENTITIES AND OTHER PARTICIPANTS

ARTICLE 7 — BENEFICIARIES

The beneficiaries, as signatories of the Agreement, are fully responsible towards the granting authority for implementing it and for complying with all its obligations.

They must implement the Agreement to their best abilities, in good faith and in accordance with all the obligations and terms and conditions it sets out.

They must have the appropriate resources to implement the action and implement the action under their own responsibility and in accordance with Article 11. If they rely on affiliated entities or other

[11] For the definition, see Article 180(2)(b) of EU Financial Regulation 2018/1046: '**operating grant**' means an EU grant to finance "the functioning of a body which has an objective forming part of and supporting an EU policy".

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participants (see Articles 8 and 9), they retain sole responsibility towards the granting authority and the other beneficiaries.

They are jointly responsible for the *technical* implementation of the action. If one of the beneficiaries fails to implement their part of the action, the other beneficiaries must ensure that this part is implemented by someone else (without being entitled to an increase of the maximum grant amount and subject to an amendment; see Article 39). The *financial* responsibility of each beneficiary in case of recoveries is governed by Article 22.

The beneficiaries (and their action) must remain eligible under the EU programme funding the grant for the entire duration of the action. Costs and contributions will be eligible only as long as the beneficiary and the action are eligible.

The **internal roles and responsibilities** of the beneficiaries are divided as follows:

(a) Each beneficiary must:

(i) keep information stored in the Portal Participant Register up to date (see Article 19)

(ii) inform the granting authority (and the other beneficiaries) immediately of any events or circumstances likely to affect significantly or delay the implementation of the action (see Article 19)

(iii) submit to the coordinator in good time:

- the prefinancing guarantees (if required; see Article 23)
- the financial statements and certificates on the financial statements (CFS) (if required; see Articles 21 and 24.2 and Data Sheet, Point 4.3)
- the contribution to the deliverables and technical reports (see Article 21)
- any other documents or information required by the granting authority under the Agreement

(iv) submit via the Portal data and information related to the participation of their affiliated entities.

(b) The coordinator must:

(i) monitor that the action is implemented properly (see Article 11)

(ii) act as the intermediary for all communications between the consortium and the granting authority, unless the Agreement or granting authority specifies otherwise, and in particular:

- submit the prefinancing guarantees to the granting authority (if any)
- request and review any documents or information required and verify their quality and completeness before passing them on to the granting authority
- submit the deliverables and reports to the granting authority

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- inform the granting authority about the payments made to the other beneficiaries (report on the distribution of payments; if required, see Articles 22 and 32)

(iii) distribute the payments received from the granting authority to the other beneficiaries without unjustified delay (see Article 22).

The coordinator may not delegate or subcontract the above-mentioned tasks to any other beneficiary or third party (including affiliated entities).

However, coordinators which are public bodies may delegate the tasks set out in Point (b)(ii) last indent and (iii) above to entities with 'authorisation to administer' which they have created or which are controlled by or affiliated to them. In this case, the coordinator retains sole responsibility for the payments and for compliance with the obligations under the Agreement.

Moreover, coordinators which are 'sole beneficiaries'[12] (or similar, such as European research infrastructure consortia (ERICs)) may delegate the tasks set out in Point (b)(i) to (iii) above to one of their members. The coordinator retains sole responsibility for compliance with the obligations under the Agreement.

The beneficiaries must have **internal arrangements** regarding their operation and co-ordination, to ensure that the action is implemented properly.

If required by the granting authority (see Data Sheet, Point 1), these arrangements must be set out in a written **consortium agreement** between the beneficiaries, covering for instance:

- the internal organisation of the consortium
- the management of access to the Portal
- different distribution keys for the payments and financial responsibilities in case of recoveries (if any)
- additional rules on rights and obligations related to background and results (see Article 16)
- settlement of internal disputes
- liability, indemnification and confidentiality arrangements between the beneficiaries.

The internal arrangements must not contain any provision contrary to this Agreement.

ARTICLE 8 — AFFILIATED ENTITIES

The following entities which are linked to a beneficiary will participate in the action as 'affiliated entities':

- **Collecteur Analyseur de Données (CAD)**, PIC 880793078, linked to INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM)

[12] For the definition, see Article 187(2) EU Financial Regulation 2018/1046: "Where several entities satisfy the criteria for being awarded a grant and together form one entity, that entity may be treated as the **sole beneficiary**, including where it is specifically established for the purpose of implementing the action financed by the grant."

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- **AGENTURA PRO ZDRAVOTNICKY VYZKUM CESKE REPUBLIKY AZV CR (AZV)**, PIC 878890229, linked to MINISTERSTVO ZDRAVOTNICTVI CESKE REPUBLIKY (MZd)

- **KLINIKUM DER UNIVERSITAT MUNCHEN (KUM)**, PIC 995625946, linked to LUDWIG-MAXIMILIANS-UNIVERSITAET MUENCHEN (LMU)

Affiliated entities can charge costs and contributions to the action under the same conditions as the beneficiaries and must implement the action tasks attributed to them in Annex 1 in accordance with Article 11.

Their costs and contributions will be included in Annex 2 and will be taken into account for the calculation of the grant.

The beneficiaries must ensure that all their obligations under this Agreement also apply to their affiliated entities.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the affiliated entities.

Breaches by affiliated entities will be handled in the same manner as breaches by beneficiaries. Recovery of undue amounts will be handled through the beneficiaries.

If the granting authority requires joint and several liability of affiliated entities (see Data Sheet, Point 4.4), they must sign the declaration set out in Annex 3a and may be held liable in case of enforced recoveries against their beneficiaries (see Article 22.2 and 22.4).

ARTICLE 9 — OTHER PARTICIPANTS INVOLVED IN THE ACTION

9.1 Associated partners

The following entities which cooperate with a beneficiary will participate in the action as ‘associated partners’:

- **ASTRAZENECA AB (AZ)**, PIC 999941379

- **CHILDREN'S HOSPITAL OF EASTERN ONTARIO RESEARCH INSTITUTE INC (CHEO-RI)**, PIC 907681187

- **CANADIAN INSTITUTES OF HEALTH RESEARCH (CIHR)**, PIC 960368386

- **DEUTSCHE FORSCHUNGSGEMEINSCHAFT EV (DFG)**, PIC 999547462

- **FUJIFILM DIOSYNTH BIOTECHNOLOGIES UK LIMITED (FDB)**, PIC 962770494

- **FONDS DE RECHERCHE DU QUEBEC - SANTE (FRQS)**, PIC 963122410

- **HIPRA HUMAN HEALTH SL (HIPRA)**, PIC 890821326

- **LABORATORIOS HIPRA SA (LAB HIPRA)**, PIC 991274041

- **MICYRN (MICYRN)**, PIC 880745451

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- **MILTENYI BIOTEC BV & CO KG (Miltenyi)**, PIC 897602402
- **PFIZER INC (Pfizer)**, PIC 887211374
- **DEPARTMENT OF HEALTH GOVERNMENT OF WESTERN AUSTRALIA (RCC)**, PIC 960480421
- **REITHERA SRL (REI)**, PIC 998129419
- **LABORATORIO REIG JOFRE SA (RJF)**, PIC 951005073
- **F. HOFFMANN-LA ROCHE AG (ROCHE)**, PIC 999601782
- **SCHWEIZERISCHER NATIONALFONDS ZUR FORDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG (SNSF)**, PIC 999540575
- **UCB BIOPHARMA (UCB)**, PIC 937666409
- **FRAUNHOFER UK RESEARCH LIMITED (Fraunhofer UK)**, PIC 952487039
- **GENETIC ALLIANCE UK LTD (GA UK)**, PIC 999790932
- **UNIVERSITY OF NEWCASTLE UPON TYNE (UNEW)**, PIC 999985417
- **Cambridge University Hospitals NHS Foundation Trust (CUH)**, PIC 991793961
- **UNIVERSITY OF LEICESTER (ULEIC)**, PIC 999985514
- **THE QUEEN'S UNIVERSITY OF BELFAST (QUB-UK)**, PIC 999992013
- **UNIVERSITY COLLEGE LONDON (UCL)**, PIC 999975620
- **THE CHANCELLOR MASTERS AND SCHOLARS OF THE UNIVERSITY OF CAMBRIDGE (UCAM)**, PIC 999977172

Associated partners must implement the action tasks attributed to them in Annex 1 in accordance with Article 11. They may not charge costs or contributions to the action and the costs for their tasks are not eligible.

The tasks must be set out in Annex 1.

The beneficiaries must ensure that their contractual obligations under Articles 11 (proper implementation), 12 (conflict of interests), 13 (confidentiality and security), 14 (ethics), 17.2 (visibility), 18 (specific rules for carrying out action), 19 (information) and 20 (record-keeping) also apply to the associated partners.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the associated partners.

9.2 Third parties giving in-kind contributions to the action

Other third parties may give in-kind contributions to the action (i.e. personnel, equipment, other goods, works and services, etc. which are free-of-charge) if necessary for the implementation.

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Third parties giving in-kind contributions do not implement any action tasks. They may not charge costs or contributions to the action, but the costs for the in-kind contributions are eligible and may be charged by the beneficiaries which use them, under the conditions set out in Article 6. The costs will be included in Annex 2 as part of the beneficiaries' costs.

The third parties and their in-kind contributions should be set out in Annex 1.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the third parties giving in-kind contributions.

9.3 Subcontractors

Subcontractors may participate in the action, if necessary for the implementation.

Subcontractors must implement their action tasks in accordance with Article 11. The costs for the subcontracted tasks (invoiced price from the subcontractor) are eligible and may be charged by the beneficiaries, under the conditions set out in Article 6. The costs will be included in Annex 2 as part of the beneficiaries' costs.

The beneficiaries must ensure that their contractual obligations under Articles 11 (proper implementation), 12 (conflict of interest), 13 (confidentiality and security), 14 (ethics), 17.2 (visibility), 18 (specific rules for carrying out action), 19 (information) and 20 (record-keeping) also apply to the subcontractors.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the subcontractors.

9.4 Recipients of financial support to third parties

If the action includes providing financial support to third parties (e.g. grants, prizes or similar forms of support), the beneficiaries must ensure that their contractual obligations under Articles 12 (conflict of interest), 13 (confidentiality and security), 14 (ethics), 17.2 (visibility), 18 (specific rules for carrying out action), 19 (information) and 20 (record-keeping)also apply to the third parties receiving the support (recipients).

The beneficiaries must also ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the recipients.

ARTICLE 10 — PARTICIPANTS WITH SPECIAL STATUS

10.1 Non-EU participants

Participants which are established in a non-EU country (if any) undertake to comply with their obligations under the Agreement and:

- to respect general principles (including fundamental rights, values and ethical principles, environmental and labour standards, rules on classified information, intellectual property rights, visibility of funding and protection of personal data)

- for the submission of certificates under Article 24: to use qualified external auditors which

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are independent and comply with comparable standards as those set out in EU Directive 2006/43/EC[13]

- for the controls under Article 25: to allow for checks, reviews, audits and investigations (including on-the-spot checks, visits and inspections) by the bodies mentioned in that Article (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.).

Special rules on dispute settlement apply (see Data Sheet, Point 5).

10.2 Participants which are international organisations

Participants which are international organisations (IOs; if any) undertake to comply with their obligations under the Agreement and:

- to respect general principles (including fundamental rights, values and ethical principles, environmental and labour standards, rules on classified information, intellectual property rights, visibility of funding and protection of personal data)

- for the submission of certificates under Article 24: to use either independent public officers or external auditors which comply with comparable standards as those set out in EU Directive 2006/43/EC

- for the controls under Article 25: to allow for the checks, reviews, audits and investigations by the bodies mentioned in that Article, taking into account the specific agreements concluded by them and the EU (if any).

For such participants, nothing in the Agreement will be interpreted as a waiver of their privileges or immunities, as accorded by their constituent documents or international law.

Special rules on applicable law and dispute settlement apply (see Article 43 and Data Sheet, Point 5).

10.3 Pillar-assessed participants

Pillar-assessed participants (if any) may rely on their own systems, rules and procedures, in so far as they have been positively assessed and do not call into question the decision awarding the grant or breach the principle of equal treatment of applicants or beneficiaries.

'Pillar-assessment' means a review by the European Commission on the systems, rules and procedures which participants use for managing EU grants (in particular internal control system, accounting system, external audits, financing of third parties, rules on recovery and exclusion, information on recipients and protection of personal data; see Article 154 EU Financial Regulation 2018/1046).

Participants with a positive pillar assessment may rely on their own systems, rules and procedures, in particular for:

- record-keeping (Article 20): may be done in accordance with internal standards, rules and procedures

[13] Directive 2006/43/EC of the European Parliament and of the Council of 17 May 2006 on statutory audits of annual accounts and consolidated accounts or similar national regulations (OJ L 157, 9.6.2006, p. 87).

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- currency conversion for financial statements (Article 21): may be done in accordance with usual accounting practices

- guarantees (Article 23): for public law bodies, prefinancing guarantees are not needed

- certificates (Article 24):

    - certificates on the financial statements (CFS): may be provided by their regular internal or external auditors and in accordance with their internal financial regulations and procedures

    - certificates on usual accounting practices (CoMUC): are not needed if those practices are covered by an ex-ante assessment

and use the following specific rules, for:

- recoveries (Article 22): in case of financial support to third parties, there will be no recovery if the participant has done everything possible to retrieve the undue amounts from the third party receiving the support (including legal proceedings) and non-recovery is not due to an error or negligence on its part

- checks, reviews, audits and investigations by the EU (Article 25): will be conducted taking into account the rules and procedures specifically agreed between them and the framework agreement (if any)

- impact evaluation (Article 26): will be conducted in accordance with the participant's internal rules and procedures and the framework agreement (if any)

- grant agreement suspension (Article 31): certain costs incurred during grant suspension are eligible (notably, minimum costs necessary for a possible resumption of the action and costs relating to contracts which were entered into before the pre-information letter was received and which could not reasonably be suspended, reallocated or terminated on legal grounds)

- grant agreement termination (Article 32): the final grant amount and final payment will be calculated taking into account also costs relating to contracts due for execution only after termination takes effect, if the contract was entered into before the pre-information letter was received and could not reasonably be terminated on legal grounds

- liability for damages (Article 33.2): the granting authority must be compensated for damage it sustains as a result of the implementation of the action or because the action was not implemented in full compliance with the Agreement only if the damage is due to an infringement of the participant's internal rules and procedures or due to a violation of third parties' rights by the participant or one of its employees or individual for whom the employees are responsible.

Participants whose pillar assessment covers procurement and granting procedures may also do purchases, subcontracting and financial support to third parties (Article 6.2) in accordance with their internal rules and procedures for purchases, subcontracting and financial support.

Participants whose pillar assessment covers data protection rules may rely on their internal standards, rules and procedures for data protection (Article 15).

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The participants may however not rely on provisions which would breach the principle of equal treatment of applicants or beneficiaries or call into question the decision awarding the grant, such as in particular:

- eligibility (Article 6)
- consortium roles and set-up (Articles 7-9)
- security and ethics (Articles 13, 14)
- IPR (including background and results, access rights and rights of use), communication, dissemination and visibility (Articles 16 and 17)
- information obligation (Article 19)
- payment, reporting and amendments (Articles 21, 22 and 39)
- rejections, reductions, suspensions and terminations (Articles 27, 28, 29-32)

If the pillar assessment was subject to remedial measures, reliance on the internal systems, rules and procedures is subject to compliance with those remedial measures.

Participants whose assessment has not yet been updated to cover (the new rules on) data protection may rely on their internal systems, rules and procedures, provided that they ensure that personal data is:

- processed lawfully, fairly and in a transparent manner in relation to the data subject
- collected for specified, explicit and legitimate purposes and not further processed in a manner that is incompatible with those purposes
- adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed
- accurate and, where necessary, kept up to date
- kept in a form which permits identification of data subjects for no longer than is necessary for the purposes for which the data is processed and
- processed in a manner that ensures appropriate security of the personal data.

Participants must inform the coordinator without delay of any changes to the systems, rules and procedures that were part of the pillar assessment. The coordinator must immediately inform the granting authority.

Pillar-assessed participants that have also concluded a framework agreement with the EU, may moreover — under the same conditions as those above (i.e. not call into question the decision awarding the grant or breach the principle of equal treatment of applicants or beneficiaries) — rely on the provisions set out in that framework agreement.

SECTION 2 RULES FOR CARRYING OUT THE ACTION

ARTICLE 11 — PROPER IMPLEMENTATION OF THE ACTION

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11.1 Obligation to properly implement the action

The beneficiaries must implement the action as described in Annex 1 and in compliance with the provisions of the Agreement, the call conditions and all legal obligations under applicable EU, international and national law.

11.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 12 — CONFLICT OF INTERESTS

12.1 Conflict of interests

The beneficiaries must take all measures to prevent any situation where the impartial and objective implementation of the Agreement could be compromised for reasons involving family, emotional life, political or national affinity, economic interest or any other direct or indirect interest (‘conflict of interests’).

They must formally notify the granting authority without delay of any situation constituting or likely to lead to a conflict of interests and immediately take all the necessary steps to rectify this situation.

The granting authority may verify that the measures taken are appropriate and may require additional measures to be taken by a specified deadline.

12.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28) and the grant or the beneficiary may be terminated (see Article 32).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 13 — CONFIDENTIALITY AND SECURITY

13.1 Sensitive information

The parties must keep confidential any data, documents or other material (in any form) that is identified as sensitive in writing (‘sensitive information’) — during the implementation of the action and for at least until the time-limit set out in the Data Sheet (see Point 6).

If a beneficiary requests, the granting authority may agree to keep such information confidential for a longer period.

Unless otherwise agreed between the parties, they may use sensitive information only to implement the Agreement.

The beneficiaries may disclose sensitive information to their personnel or other participants involved in the action only if they:

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(a) need to know it in order to implement the Agreement and

(b) are bound by an obligation of confidentiality.

The granting authority may disclose sensitive information to its staff and to other EU institutions and bodies.

It may moreover disclose sensitive information to third parties, if:

(a) this is necessary to implement the Agreement or safeguard the EU financial interests and

(b) the recipients of the information are bound by an obligation of confidentiality.

The confidentiality obligations no longer apply if:

(a) the disclosing party agrees to release the other party

(b) the information becomes publicly available, without breaching any confidentiality obligation

(c) the disclosure of the sensitive information is required by EU, international or national law.

Specific confidentiality rules (if any) are set out in Annex 5.

13.2 Classified information

The parties must handle classified information in accordance with the applicable EU, international or national law on classified information (in particular, Decision 2015/444[14] and its implementing rules).

Deliverables which contain classified information must be submitted according to special procedures agreed with the granting authority.

Action tasks involving classified information may be subcontracted only after explicit approval (in writing) from the granting authority.

Classified information may not be disclosed to any third party (including participants involved in the action implementation) without prior explicit written approval from the granting authority.

Specific security rules (if any) are set out in Annex 5.

13.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 14 — ETHICS AND VALUES

14.1 Ethics

[14] Commission Decision 2015/444/EC, Euratom of 13 March 2015 on the security rules for protecting EU classified information (OJ L 72, 17.3.2015, p. 53).

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The action must be carried out in line with the highest ethical standards and the applicable EU, international and national law on ethical principles.

Specific ethics rules (if any) are set out in Annex 5.

14.2 Values

The beneficiaries must commit to and ensure the respect of basic EU values (such as respect for human dignity, freedom, democracy, equality, the rule of law and human rights, including the rights of minorities).

Specific rules on values (if any) are set out in Annex 5.

14.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 15 — DATA PROTECTION

15.1 Data processing by the granting authority

Any personal data under the Agreement will be processed under the responsibility of the data controller of the granting authority in accordance with and for the purposes set out in the Portal Privacy Statement.

For grants where the granting authority is the European Commission, an EU regulatory or executive agency, joint undertaking or other EU body, the processing will be subject to Regulation 2018/1725[15].

15.2 Data processing by the beneficiaries

The beneficiaries must process personal data under the Agreement in compliance with the applicable EU, international and national law on data protection (in particular, Regulation 2016/679[16]).

They must ensure that personal data is:

- processed lawfully, fairly and in a transparent manner in relation to the data subjects
- collected for specified, explicit and legitimate purposes and not further processed in a manner that is incompatible with those purposes

[15] Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC (OJ L 295, 21.11.2018, p. 39).

[16] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (‘GDPR’) (OJ L 119, 4.5.2016, p. 1).

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- adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed
- accurate and, where necessary, kept up to date
- kept in a form which permits identification of data subjects for no longer than is necessary for the purposes for which the data is processed and
- processed in a manner that ensures appropriate security of the data.

The beneficiaries may grant their personnel access to personal data only if it is strictly necessary for implementing, managing and monitoring the Agreement. The beneficiaries must ensure that the personnel is under a confidentiality obligation.

The beneficiaries must inform the persons whose data are transferred to the granting authority and provide them with the Portal Privacy Statement.

15.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 16 — INTELLECTUAL PROPERTY RIGHTS (IPR) — BACKGROUND AND RESULTS —ACCESS RIGHTS AND RIGHTS OF USE

16.1 Background and access rights to background

The beneficiaries must give each other and the other participants access to the background identified as needed for implementing the action, subject to any specific rules in Annex 5.

‘Background’ means any data, know-how or information — whatever its form or nature (tangible or intangible), including any rights such as intellectual property rights — that is:

(a) held by the beneficiaries before they acceded to the Agreement and

(b) needed to implement the action or exploit the results.

If background is subject to rights of a third party, the beneficiary concerned must ensure that it is able to comply with its obligations under the Agreement.

16.2 Ownership of results

The granting authority does not obtain ownership of the results produced under the action.

‘Results’ means any tangible or intangible effect of the action, such as data, know-how or information, whatever its form or nature, whether or not it can be protected, as well as any rights attached to it, including intellectual property rights.

16.3 Rights of use of the granting authority on materials, documents and information received for policy, information, communication, dissemination and publicity purposes

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The granting authority has the right to use non-sensitive information relating to the action and materials and documents received from the beneficiaries (notably summaries for publication, deliverables, as well as any other material, such as pictures or audio-visual material, in paper or electronic form) for policy, information, communication, dissemination and publicity purposes — during the action or afterwards.

The right to use the beneficiaries' materials, documents and information is granted in the form of a royalty-free, non-exclusive and irrevocable licence, which includes the following rights:

(a) **use for its own purposes** (in particular, making them available to persons working for the granting authority or any other EU service (including institutions, bodies, offices, agencies, etc.) or EU Member State institution or body; copying or reproducing them in whole or in part, in unlimited numbers; and communication through press information services)

(b) **distribution to the public** (in particular, publication as hard copies and in electronic or digital format, publication on the internet, as a downloadable or non-downloadable file, broadcasting by any channel, public display or presentation, communicating through press information services, or inclusion in widely accessible databases or indexes)

(c) **editing or redrafting** (including shortening, summarising, inserting other elements (e.g. meta-data, legends, other graphic, visual, audio or text elements), extracting parts (e.g. audio or video files), dividing into parts, use in a compilation)

(d) **translation**

(e) **storage** in paper, electronic or other form

(f) **archiving**, in line with applicable document-management rules

(g) the right to authorise **third parties** to act on its behalf or sub-license to third parties the modes of use set out in Points (b), (c), (d) and (f), if needed for the information, communication and publicity activity of the granting authority

(h) **processing**, analysing, aggregating the materials, documents and information received and **producing derivative works**.

The rights of use are granted for the whole duration of the industrial or intellectual property rights concerned.

If materials or documents are subject to moral rights or third party rights (including intellectual property rights or rights of natural persons on their image and voice), the beneficiaries must ensure that they comply with their obligations under this Agreement (in particular, by obtaining the necessary licences and authorisations from the rights holders concerned).

Where applicable, the granting authority will insert the following information:

> "© – [year] – [name of the copyright owner]. All rights reserved. Licensed to the [name of granting authority] under conditions."

16.4 Specific rules on IPR, results and background

Specific rules regarding intellectual property rights, results and background (if any) are set out in Annex 5.

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16.5 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such a breach may also lead to other measures described in Chapter 5.

ARTICLE 17 — COMMUNICATION, DISSEMINATION AND VISIBILITY

17.1 Communication — Dissemination — Promoting the action

Unless otherwise agreed with the granting authority, the beneficiaries must promote the action and its results by providing targeted information to multiple audiences (including the media and the public), in accordance with Annex 1 and in a strategic, coherent and effective manner.

Before engaging in a communication or dissemination activity expected to have a major media impact, the beneficiaries must inform the granting authority.

17.2 Visibility — European flag and funding statement

Unless otherwise agreed with the granting authority, communication activities of the beneficiaries related to the action (including media relations, conferences, seminars, information material, such as brochures, leaflets, posters, presentations, etc., in electronic form, via traditional or social media, etc.), dissemination activities and any infrastructure, equipment, vehicles, supplies or major result funded by the grant must acknowledge EU support and display the European flag (emblem) and funding statement (translated into local languages, where appropriate):







Funded by the
European Union



Co-funded by the
European Union

The emblem must remain distinct and separate and cannot be modified by adding other visual marks, brands or text.

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Apart from the emblem, no other visual identity or logo may be used to highlight the EU support.

When displayed in association with other logos (e.g. of beneficiaries or sponsors), the emblem must be displayed at least as prominently and visibly as the other logos.

For the purposes of their obligations under this Article, the beneficiaries may use the emblem without first obtaining approval from the granting authority. This does not, however, give them the right to exclusive use. Moreover, they may not appropriate the emblem or any similar trademark or logo, either by registration or by any other means.

17.3 Quality of information — Disclaimer

Any communication or dissemination activity related to the action must use factually accurate information.

Moreover, it must indicate the following disclaimer (translated into local languages where appropriate):

> "Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or [name of the granting authority]. Neither the European Union nor the granting authority can be held responsible for them."

17.4 Specific communication, dissemination and visibility rules

Specific communication, dissemination and visibility rules (if any) are set out in Annex 5.

17.5 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 18 — SPECIFIC RULES FOR CARRYING OUT THE ACTION

18.1 Specific rules for carrying out the action

Specific rules for implementing the action (if any) are set out in Annex 5.

18.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such a breach may also lead to other measures described in Chapter 5.

SECTION 3 GRANT ADMINISTRATION

ARTICLE 19 — GENERAL INFORMATION OBLIGATIONS

19.1 Information requests

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The beneficiaries must provide — during the action or afterwards and in accordance with Article 7 — any information requested in order to verify eligibility of the costs or contributions declared, proper implementation of the action and compliance with the other obligations under the Agreement.

The information provided must be accurate, precise and complete and in the format requested, including electronic format.

19.2 Participant Register data updates

The beneficiaries must keep — at all times, during the action or afterwards — their information stored in the Portal Participant Register up to date, in particular, their name, address, legal representatives, legal form and organisation type.

19.3 Information about events and circumstances which impact the action

The beneficiaries must immediately inform the granting authority (and the other beneficiaries) of any of the following:

(a) **events** which are likely to affect or delay the implementation of the action or affect the EU's financial interests, in particular:

(i) changes in their legal, financial, technical, organisational or ownership situation (including changes linked to one of the exclusion grounds listed in the declaration of honour signed before grant signature)

(ii) linked action information: not applicable

(b) **circumstances** affecting:

(i) the decision to award the grant or

(ii) compliance with requirements under the Agreement.

19.4 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 20 — RECORD-KEEPING

20.1 Keeping records and supporting documents

The beneficiaries must — at least until the time-limit set out in the Data Sheet (see Point 6) — keep records and other supporting documents to prove the proper implementation of the action in line with the accepted standards in the respective field (if any).

In addition, the beneficiaries must — for the same period — keep the following to justify the amounts declared:

(a) for actual costs: adequate records and supporting documents to prove the costs declared (such

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as contracts, subcontracts, invoices and accounting records); in addition, the beneficiaries' usual accounting and internal control procedures must enable direct reconciliation between the amounts declared, the amounts recorded in their accounts and the amounts stated in the supporting documents

(b) for flat-rate costs and contributions (if any): adequate records and supporting documents to prove the eligibility of the costs or contributions to which the flat-rate is applied

(c) for the following simplified costs and contributions: the beneficiaries do not need to keep specific records on the actual costs incurred, but must keep:

(i) for unit costs and contributions (if any): adequate records and supporting documents to prove the number of units declared

(ii) for lump sum costs and contributions (if any): adequate records and supporting documents to prove proper implementation of the work as described in Annex 1

(iii) for financing not linked to costs (if any): adequate records and supporting documents to prove the achievement of the results or the fulfilment of the conditions as described in Annex 1

(d) for unit, flat-rate and lump sum costs and contributions according to usual cost accounting practices (if any): the beneficiaries must keep any adequate records and supporting documents to prove that their cost accounting practices have been applied in a consistent manner, based on objective criteria, regardless of the source of funding, and that they comply with the eligibility conditions set out in Articles 6.1 and 6.2.

Moreover, the following is needed for specific budget categories:

(e) for personnel costs: time worked for the beneficiary under the action must be supported by declarations signed monthly by the person and their supervisor, unless another reliable time-record system is in place; the granting authority may accept alternative evidence supporting the time worked for the action declared, if it considers that it offers an adequate level of assurance

(f) additional record-keeping rules: not applicable

The records and supporting documents must be made available upon request (see Article 19) or in the context of checks, reviews, audits or investigations (see Article 25).

If there are on-going checks, reviews, audits, investigations, litigation or other pursuits of claims under the Agreement (including the extension of findings; see Article 25), the beneficiaries must keep these records and other supporting documentation until the end of these procedures.

The beneficiaries must keep the original documents. Digital and digitalised documents are considered originals if they are authorised by the applicable national law. The granting authority may accept non-original documents if they offer a comparable level of assurance.

20.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, costs or contributions insufficiently

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substantiated will be ineligible (see Article 6) and will be rejected (see Article 27), and the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 21 — REPORTING

21.1 Continuous reporting

The beneficiaries must continuously report on the progress of the action (e.g. **deliverables, milestones, outputs/outcomes, critical risks, indicators,** etc; if any), in the Portal Continuous Reporting tool and in accordance with the timing and conditions it sets out (as agreed with the granting authority).

Standardised deliverables (e.g. progress reports not linked to payments, reports on cumulative expenditure, special reports, etc; if any) must be submitted using the templates published on the Portal.

21.2 Periodic reporting: Technical reports and financial statements

In addition, the beneficiaries must provide reports to request payments, in accordance with the schedule and modalities set out in the Data Sheet (see Point 4.2):

- for additional prefinancings (if any): an **additional prefinancing report**
- for interim payments (if any) and the final payment: a **periodic report**.

The prefinancing and periodic reports include a technical and financial part.

The technical part includes an overview of the action implementation. It must be prepared using the template available in the Portal Periodic Reporting tool.

The financial part of the additional prefinancing report includes a statement on the use of the previous prefinancing payment.

The financial part of the periodic report includes:

- the financial statements (individual and consolidated; for all beneficiaries/affiliated entities)
- the explanation on the use of resources (or detailed cost reporting table, if required)
- the certificates on the financial statements (CFS) (if required; see Article 24.2 and Data Sheet, Point 4.3).

The **financial statements** must detail the eligible costs and contributions for each budget category and, for the final payment, also the revenues for the action (see Articles 6 and 22).

All eligible costs and contributions incurred should be declared, even if they exceed the amounts indicated in the estimated budget (see Annex 2). Amounts that are not declared in the individual financial statements will not be taken into account by the granting authority.

By signing the financial statements (directly in the Portal Periodic Reporting tool), the beneficiaries confirm that:

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- the information provided is complete, reliable and true
- the costs and contributions declared are eligible (see Article 6)
- the costs and contributions can be substantiated by adequate records and supporting documents (see Article 20) that will be produced upon request (see Article 19) or in the context of checks, reviews, audits and investigations (see Article 25)
- for the final periodic report: all the revenues have been declared (if required; see Article 22).

Beneficiaries will have to submit also the financial statements of their affiliated entities (if any). In case of recoveries (see Article 22), beneficiaries will be held responsible also for the financial statements of their affiliated entities.

21.3 Currency for financial statements and conversion into euros

The financial statements must be drafted in euro.

Beneficiaries with general accounts established in a currency other than the euro must convert the costs recorded in their accounts into euro, at the average of the daily exchange rates published in the C series of the *Official Journal of the European Union* (ECB website), calculated over the corresponding reporting period.

If no daily euro exchange rate is published in the *Official Journal* for the currency in question, they must be converted at the average of the monthly accounting exchange rates published on the European Commission website (InforEuro), calculated over the corresponding reporting period.

Beneficiaries with general accounts in euro must convert costs incurred in another currency into euro according to their usual accounting practices.

21.4 Reporting language

The reporting must be in the language of the Agreement, unless otherwise agreed with the granting authority (see Data Sheet, Point 4.2).

21.5 Consequences of non-compliance

If a report submitted does not comply with this Article, the granting authority may suspend the payment deadline (see Article 29) and apply other measures described in Chapter 5.

If the coordinator breaches its reporting obligations, the granting authority may terminate the grant or the coordinator's participation (see Article 32) or apply other measures described in Chapter 5.

ARTICLE 22 — PAYMENTS AND RECOVERIES — CALCULATION OF AMOUNTS DUE

22.1 Payments and payment arrangements

Payments will be made in accordance with the schedule and modalities set out in the Data Sheet (see Point 4.2).

They will be made in euro to the bank account indicated by the coordinator (see Data Sheet, Point 4.2)

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and must be distributed without unjustified delay (restrictions may apply to distribution of the initial prefinancing payment; see Data Sheet, Point 4.2).

Payments to this bank account will discharge the granting authority from its payment obligation.

The cost of payment transfers will be borne as follows:

- the granting authority bears the cost of transfers charged by its bank
- the beneficiary bears the cost of transfers charged by its bank
- the party causing a repetition of a transfer bears all costs of the repeated transfer.

Payments by the granting authority will be considered to have been carried out on the date when they are debited to its account.

22.2 Recoveries

Recoveries will be made, if — at beneficiary termination, final payment or afterwards — it turns out that the granting authority has paid too much and needs to recover the amounts undue.

Each beneficiary's financial responsibility in case of recovery is in principle limited to their own debt and undue amounts of their affiliated entities.

In case of enforced recoveries (see Article 22.4), affiliated entities will be held liable for repaying debts of their beneficiaries, if required by the granting authority (see Data Sheet, Point 4.4).

22.3 Amounts due

22.3.1 Prefinancing payments

The aim of the prefinancing is to provide the beneficiaries with a float.

It remains the property of the EU until the final payment.

For **initial prefinancings** (if any), the amount due, schedule and modalities are set out in the Data Sheet (see Point 4.2).

For **additional prefinancings** (if any), the amount due, schedule and modalities are also set out in the Data Sheet (see Point 4.2). However, if the statement on the use of the previous prefinancing payment shows that less than 70% was used, the amount set out in the Data Sheet will be reduced by the difference between the 70% threshold and the amount used.

The contribution to the Mutual Insurance Mechanism will be retained from the prefinancing payments (at the rate and in accordance with the modalities set out in the Data Sheet, see Point 4.2) and transferred to the Mechanism.

Prefinancing payments (or parts of them) may be offset (without the beneficiaries' consent) against amounts owed by a beneficiary to the granting authority — up to the amount due to that beneficiary.

For grants where the granting authority is the European Commission or an EU executive agency, offsetting may also be done against amounts owed to other Commission services or executive agencies.

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Payments will not be made if the payment deadline or payments are suspended (see Articles 29 and 30).

22.3.2 Amount due at beneficiary termination — Recovery

In case of beneficiary termination, the granting authority will determine the provisional amount due for the beneficiary concerned. Payments (if any) will be made with the next interim or final payment.

The **amount due** will be calculated in the following step:

Step 1 — Calculation of the total accepted EU contribution

Step 1 — Calculation of the total accepted EU contribution

The granting authority will first calculate the 'accepted EU contribution' for the beneficiary for all reporting periods, by calculating the 'maximum EU contribution to costs' (applying the funding rate to the accepted costs of the beneficiary), taking into account requests for a lower contribution to costs and CFS threshold cappings (if any; see Article 24.5) and adding the contributions (accepted unit, flat-rate or lump sum contributions and financing not linked to costs, if any).

After that, the granting authority will take into account grant reductions (if any). The resulting amount is the 'total accepted EU contribution' for the beneficiary.

The **balance** is then calculated by deducting the payments received (if any; see report on the distribution of payments in Article 32), from the total accepted EU contribution:

{total accepted EU contribution for the beneficiary

minus

{prefinancing and interim payments received (if any)}}.

If the balance is **positive**, the amount will be included in the next interim or final payment to the consortium.

If the balance is **negative**, it will be **recovered** in accordance with the following procedure:

The granting authority will send a **pre-information letter** to the beneficiary concerned:

- formally notifying the intention to recover, the amount due, the amount to be recovered and the reasons why and
- requesting observations within 30 days of receiving notification.

If no observations are submitted (or the granting authority decides to pursue recovery despite the observations it has received), it will confirm the amount to be recovered and ask this amount to be paid to the coordinator (**confirmation letter**).

If payment is not made to the coordinator by the date specified in the confirmation letter, the granting authority may call on the Mutual Insurance Mechanism to intervene, if continuation of the action is guaranteed and the conditions set out in the rules governing the Mechanism are met.

In this case, it will send a **beneficiary recovery letter**, together with a **debit note** with the terms and date for payment.

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The debit note for the beneficiary will include the amount calculated for the affiliated entities which also had to end their participation (if any).

If payment is not made by the date specified in the debit note, the granting authority will **enforce recovery** in accordance with Article 22.4.

The amounts will later on also be taken into account for the next interim or final payment.

22.3.3 Interim payments

Interim payments reimburse the eligible costs and contributions claimed for the implementation of the action during the reporting periods (if any).

Interim payments (if any) will be made in accordance with the schedule and modalities set out the Data Sheet (see Point 4.2).

Payment is subject to the approval of the periodic report. Its approval does not imply recognition of compliance, authenticity, completeness or correctness of its content.

The **interim payment** will be calculated by the granting authority in the following steps:

Step 1 — Calculation of the total accepted EU contribution

Step 2 — Limit to the interim payment ceiling

Step 1 — Calculation of the total accepted EU contribution

The granting authority will calculate the 'accepted EU contribution' for the action for the reporting period, by first calculating the 'maximum EU contribution to costs' (applying the funding rate to the accepted costs of each beneficiary), taking into account requests for a lower contribution to costs, and CFS threshold cappings (if any; see Article 24.5) and adding the contributions (accepted unit, flat-rate or lump sum contributions and financing not linked to costs, if any).

After that, the granting authority will take into account grant reductions from beneficiary termination (if any). The resulting amount is the 'total accepted EU contribution'.

Step 2 — Limit to the interim payment ceiling

The resulting amount is then capped to ensure that the total amount of prefinancing and interim payments (if any) does not exceed the interim payment ceiling set out in the Data Sheet (see Point 4.2).

Interim payments (or parts of them) may be offset (without the beneficiaries' consent) against amounts owed by a beneficiary to the granting authority — up to the amount due to that beneficiary.

For grants where the granting authority is the European Commission or an EU executive agency, offsetting may also be done against amounts owed to other Commission services or executive agencies.

Payments will not be made if the payment deadline or payments are suspended (see Articles 29 and 30).

22.3.4 Final payment — Final grant amount — Revenues and Profit — Recovery

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The final payment (payment of the balance) reimburses the remaining part of the eligible costs and contributions claimed for the implementation of the action (if any).

The final payment will be made in accordance with the schedule and modalities set out in the Data Sheet (see Point 4.2).

Payment is subject to the approval of the final periodic report. Its approval does not imply recognition of compliance, authenticity, completeness or correctness of its content.

The **final grant amount for the action** will be calculated in the following steps:

Step 1 — Calculation of the total accepted EU contribution

Step 2 — Limit to the maximum grant amount

Step 3 — Reduction due to the no-profit rule

Step 1 — Calculation of the total accepted EU contribution

The granting authority will first calculate the 'accepted EU contribution' for the action for all reporting periods, by calculating the 'maximum EU contribution to costs' (applying the funding rate to the total accepted costs of each beneficiary), taking into account requests for a lower contribution to costs, CFS threshold cappings (if any; see Article 24.5) and adding the contributions (accepted unit, flat-rate or lump sum contributions and financing not linked to costs, if any).

After that, the granting authority will take into account grant reductions (if any). The resulting amount is the 'total accepted EU contribution'.

Step 2 — Limit to the maximum grant amount

If the resulting amount is higher than the maximum grant amount set out in Article 5.2, it will be limited to the latter.

Step 3 — Reduction due to the no-profit rule

If the no-profit rule is provided for in the Data Sheet (see Point 4.2), the grant must not produce a profit (i.e. surplus of the amount obtained following Step 2 plus the action's revenues, over the eligible costs and contributions approved by the granting authority).

'Revenue' is all income generated by the action, during its duration (see Article 4), for beneficiaries that are profit legal entities (— with the exception of income generated by the exploitation of results, which are not considered as revenues).

If there is a profit, it will be deducted in proportion to the final rate of reimbursement of the eligible costs approved by the granting authority (as compared to the amount calculated following Steps 1 and 2 minus the contributions).

The **balance** (final payment) is then calculated by deducting the total amount of prefinancing and interim payments already made (if any), from the final grant amount:

{final grant amount

minus

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{prefinancing and interim payments made (if any)}}.

If the balance is **positive**, it will be **paid** to the coordinator.

The amount retained for the Mutual Insurance Mechanism (see above) will be released and **paid** to the coordinator (in accordance with the rules governing the Mechanism).

The final payment (or part of it) may be offset (without the beneficiaries' consent) against amounts owed by a beneficiary to the granting authority — up to the amount due to that beneficiary.

For grants where the granting authority is the European Commission or an EU executive agency, offsetting may also be done against amounts owed to other Commission services or executive agencies.

Payments will not be made if the payment deadline or payments are suspended (see Articles 29 and 30).

If — despite the release of the Mutual Insurance Mechanism contribution — the balance is **negative**, it will be **recovered** in accordance with the following procedure:

The granting authority will send a **pre-information letter** to the coordinator:

- formally notifying the intention to recover, the final grant amount, the amount to be recovered and the reasons why
- requesting a report on the distribution of payments to the beneficiaries within 30 days of receiving notification and
- requesting observations within 30 days of receiving notification.

If no observations are submitted (or the granting authority decides to pursue recovery despite the observations it has received) and the coordinator has submitted the report on the distribution of payments, it will calculate the **share of the debt per beneficiary**, by:

(a) identifying the beneficiaries for which the amount calculated as follows is negative:

{{{total accepted EU contribution for the beneficiary

divided by

total accepted EU contribution for the action}

multiplied by

final grant amount for the action},

minus

{prefinancing and interim payments received by the beneficiary (if any)}}

and

(b) dividing the debt:

{{amount calculated according to point (a) for the beneficiary concerned

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divided by

the sum of the amounts calculated according to point (a) for all the beneficiaries identified according to point (a)}

multiplied by

the amount to be recovered}.

and confirm the amount to be recovered from each beneficiary concerned (**confirmation letter**), together with **debit notes** with the terms and date for payment.

The debit notes for beneficiaries will include the amounts calculated for their affiliated entities (if any).

If the coordinator has not submitted the report on the distribution of payments, the granting authority will **recover** the full amount from the coordinator (**confirmation letter** and **debit note** with the terms and date for payment).

If payment is not made by the date specified in the debit note, the granting authority will **enforce recovery** in accordance with Article 22.4.

22.3.5 Audit implementation after final payment — Revised final grant amount — Recovery

If — after the final payment (in particular, after checks, reviews, audits or investigations; see Article 25) — the granting authority rejects costs or contributions (see Article 27) or reduces the grant (see Article 28), it will calculate the **revised final grant amount** for the beneficiary concerned.

The **beneficiary revised final grant amount** will be calculated in the following step:

Step 1 — Calculation of the revised total accepted EU contribution

Step 1 — Calculation of the revised total accepted EU contribution

The granting authority will first calculate the 'revised accepted EU contribution' for the beneficiary, by calculating the 'revised accepted costs' and 'revised accepted contributions'.

After that, it will take into account grant reductions (if any). The resulting 'revised total accepted EU contribution' is the beneficiary revised final grant amount.

If the revised final grant amount is lower than the beneficiary's final grant amount (i.e. its share in the final grant amount for the action), it will be **recovered** in accordance with the following procedure:

The **beneficiary final grant amount** (i.e. share in the final grant amount for the action) is calculated as follows:

{{total accepted EU contribution for the beneficiary

divided by

total accepted EU contribution for the action}

multiplied by

final grant amount for the action}.

The granting authority will send a **pre-information letter** to the beneficiary concerned:

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- formally notifying the intention to recover, the amount to be recovered and the reasons why and
- requesting observations within 30 days of receiving notification.

If no observations are submitted (or the granting authority decides to pursue recovery despite the observations it has received), it will confirm the amount to be recovered (**confirmation letter**), together with a **debit note** with the terms and the date for payment.

Recoveries against affiliated entities (if any) will be handled through their beneficiaries.

If payment is not made by the date specified in the debit note, the granting authority will **enforce recovery** in accordance with Article 22.4.

22.4 Enforced recovery

If payment is not made by the date specified in the debit note, the amount due will be recovered:

(a) by offsetting the amount — without the coordinator or beneficiary's consent — against any amounts owed to the coordinator or beneficiary by the granting authority.

In exceptional circumstances, to safeguard the EU financial interests, the amount may be offset before the payment date specified in the debit note.

For grants where the granting authority is the European Commission or an EU executive agency, debts may also be offset against amounts owed by other Commission services or executive agencies.

(b) financial guarantee(s): not applicable

(c) joint and several liability of beneficiaries: not applicable

(d) by holding affiliated entities jointly and severally liable (if any, see Data Sheet, Point 4.4)

(e) by taking legal action (see Article 43) or, provided that the granting authority is the European Commission or an EU executive agency, by adopting an enforceable decision under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 100(2) of EU Financial Regulation 2018/1046.

If the Mutual Insurance Mechanism was called on by the granting authority to intervene, recovery will be continued in the name of the Mutual Insurance Mechanism. If two debit notes were sent, the second one (in the name of the Mutual Insurance Mechanism) will be considered to replace the first one (in the name of the granting authority). Where the MIM intervened, offsetting, enforceable decisions or any other of the above-mentioned forms of enforced recovery may be used mutatis mutandis.

The amount to be recovered will be increased by **late-payment interest** at the rate set out in Article 22.5, from the day following the payment date in the debit note, up to and including the date the full payment is received.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

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Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2015/2366[17] applies.

For grants where the granting authority is an EU executive agency, enforced recovery by offsetting or enforceable decision will be done by the services of the European Commission (see also Article 43).

22.5 Consequences of non-compliance

22.5.1 If the granting authority does not pay within the payment deadlines (see above), the beneficiaries are entitled to **late-payment interest** at the rate applied by the European Central Bank (ECB) for its main refinancing operations in euros ('reference rate'), plus the rate specified in the Data Sheet (Point 4.2). The reference rate is the rate in force on the first day of the month in which the payment deadline expires, as published in the C series of the *Official Journal of the European Union*.

If the late-payment interest is lower than or equal to EUR 200, it will be paid to the coordinator only on request submitted within two months of receiving the late payment.

Late-payment interest is not due if all beneficiaries are EU Member States (including regional and local government authorities or other public bodies acting on behalf of a Member State for the purpose of this Agreement).

If payments or the payment deadline are suspended (see Articles 29 and 30), payment will not be considered as late.

Late-payment interest covers the period running from the day following the due date for payment (see above), up to and including the date of payment.

Late-payment interest is not considered for the purposes of calculating the final grant amount.

22.5.2 If the coordinator breaches any of its obligations under this Article, the grant may be reduced (see Article 28) and the grant or the coordinator may be terminated (see Article 32).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 23 — GUARANTEES

Not applicable

ARTICLE 24 — CERTIFICATES

24.1 Operational verification report (OVR)

Not applicable

24.2 Certificate on the financial statements (CFS)

If required by the granting authority (see Data Sheet, Point 4.3), the beneficiaries must provide

[17] Directive (EU) 2015/2366 of the European Parliament and of the Council of 25 November 2015 on payment services in the internal market, amending Directives 2002/65/EC, 2009/110/EC and 2013/36/EU and Regulation (EU) No 1093/2010, and repealing Directive 2007/64/EC (OJ L 337, 23.12.2015, p. 35).

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certificates on their financial statements (CFS), in accordance with the schedule, threshold and conditions set out in the Data Sheet.

The coordinator must submit them as part of the periodic report (see Article 21).

The certificates must be drawn up using the template published on the Portal, cover the costs declared on the basis of actual costs and costs according to usual cost accounting practices (if any), and fulfil the following conditions:

(a) be provided by a qualified approved external auditor which is independent and complies with Directive 2006/43/EC[18] (or for public bodies: by a competent independent public officer)

(b) the verification must be carried out according to the highest professional standards to ensure that the financial statements comply with the provisions under the Agreement and that the costs declared are eligible.

The certificates will not affect the granting authority's right to carry out its own checks, reviews or audits, nor preclude the European Court of Auditors (ECA), the European Public Prosecutor's Office (EPPO) or the European Anti-Fraud Office (OLAF) from using their prerogatives for audits and investigations under the Agreement (see Article 25).

If the costs (or a part of them) were already audited by the granting authority, these costs do not need to be covered by the certificate and will not be counted for calculating the threshold (if any).

24.3 Certificate on the compliance of usual cost accounting practices (CoMUC)

Not applicable

24.4 Systems and process audit (SPA)

Beneficiaries which:

- use unit, flat rate or lump sum costs or contributions according to documented (i.e. formally approved and in writing) usual costs accounting practices (if any) or
- have formalised documentation on the systems and processes for calculating their costs and contributions (i.e. formally approved and in writing), have participated in at least 150 actions under Horizon 2020 or the Euratom Research and Training Programme (2014-2018 or 2019-2020) and participate in at least 3 ongoing actions under Horizon Europe or the Euratom Research and Training Programme (2021-2025 or 2026-2027)

may apply to the granting authority for a systems and process audit (SPA).

This audit will be carried out as follows:

Step 1 – Application by the beneficiary.

Step 2 – If the application is accepted, the granting authority will carry out the systems and process

[18] Directive 2006/43/EC of the European Parliament and of the Council of 17 May 2006 on statutory audits of annual accounts and consolidated accounts or similar national regulations (OJ L 157, 9.6.2006, p. 87).

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audit, complemented by an audit of transactions (on a sample of the beneficiary's Horizon Europe or the Euratom Research and Training Programme financial statements).

Step 3 – The audit result will take the form of a risk assessment classification for the beneficiary: low, medium or high.

Low-risk beneficiaries will benefit from less (or less in-depth) ex-post audits (see Article 25) and a higher threshold for submitting certificates on the financial statements (CFS; see Articles 21 and 24.2 and Data Sheet, Point 4.3).

24.5 Consequences of non-compliance

If a beneficiary does not submit a certificate on the financial statements (CFS) or the certificate is rejected, the accepted EU contribution to costs will be capped to reflect the CFS threshold.

If a beneficiary breaches any of its other obligations under this Article, the granting authority may apply the measures described in Chapter 5.

ARTICLE 25 — CHECKS, REVIEWS, AUDITS AND INVESTIGATIONS — EXTENSION OF FINDINGS

25.1 Granting authority checks, reviews and audits

25.1.1 Internal checks

The granting authority may — during the action or afterwards — check the proper implementation of the action and compliance with the obligations under the Agreement, including assessing costs and contributions, deliverables and reports.

25.1.2 Project reviews

The granting authority may carry out reviews on the proper implementation of the action and compliance with the obligations under the Agreement (general project reviews or specific issues reviews).

Such project reviews may be started during the implementation of the action and until the time-limit set out in the Data Sheet (see Point 6). They will be formally notified to the coordinator or beneficiary concerned and will be considered to start on the date of the notification.

If needed, the granting authority may be assisted by independent, outside experts. If it uses outside experts, the coordinator or beneficiary concerned will be informed and have the right to object on grounds of commercial confidentiality or conflict of interest.

The coordinator or beneficiary concerned must cooperate diligently and provide — within the deadline requested — any information and data in addition to deliverables and reports already submitted (including information on the use of resources). The granting authority may request beneficiaries to provide such information to it directly. Sensitive information and documents will be treated in accordance with Article 13.

The coordinator or beneficiary concerned may be requested to participate in meetings, including with the outside experts.

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For **on-the-spot visits**, the beneficiary concerned must allow access to sites and premises (including to the outside experts) and must ensure that information requested is readily available.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

On the basis of the review findings, a **project review report** will be drawn up.

The granting authority will formally notify the project review report to the coordinator or beneficiary concerned, which has 30 days from receiving notification to make observations.

Project reviews (including project review reports) will be in the language of the Agreement, unless otherwise agreed with the granting authority (see Data Sheet, Point 4.2).

25.1.3 Audits

The granting authority may carry out audits on the proper implementation of the action and compliance with the obligations under the Agreement.

Such audits may be started during the implementation of the action and until the time-limit set out in the Data Sheet (see Point 6). They will be formally notified to the beneficiary concerned and will be considered to start on the date of the notification.

The granting authority may use its own audit service, delegate audits to a centralised service or use external audit firms. If it uses an external firm, the beneficiary concerned will be informed and have the right to object on grounds of commercial confidentiality or conflict of interest.

The beneficiary concerned must cooperate diligently and provide — within the deadline requested — any information (including complete accounts, individual salary statements or other personal data) to verify compliance with the Agreement. Sensitive information and documents will be treated in accordance with Article 13.

For **on-the-spot** visits, the beneficiary concerned must allow access to sites and premises (including for the external audit firm) and must ensure that information requested is readily available.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

On the basis of the audit findings, a **draft audit report** will be drawn up.

The auditors will formally notify the draft audit report to the beneficiary concerned, which has 30 days from receiving notification to make observations (contradictory audit procedure).

The **final audit report** will take into account observations by the beneficiary concerned and will be formally notified to them.

Audits (including audit reports) will be in the language of the Agreement, unless otherwise agreed with the granting authority (see Data Sheet, Point 4.2).

25.2 European Commission checks, reviews and audits in grants of other granting authorities

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Where the granting authority is not the European Commission, the latter has the same rights of checks, reviews and audits as the granting authority.

25.3 Access to records for assessing simplified forms of funding

The beneficiaries must give the European Commission access to their statutory records for the periodic assessment of simplified forms of funding which are used in EU programmes.

25.4 OLAF, EPPO and ECA audits and investigations

The following bodies may also carry out checks, reviews, audits and investigations — during the action or afterwards:

- the European Anti-Fraud Office (OLAF) under Regulations No 883/2013[19] and No 2185/96[20]
- the European Public Prosecutor's Office (EPPO) under Regulation 2017/1939
- the European Court of Auditors (ECA) under Article 287 of the Treaty on the Functioning of the EU (TFEU) and Article 257 of EU Financial Regulation 2018/1046.

If requested by these bodies, the beneficiary concerned must provide full, accurate and complete information in the format requested (including complete accounts, individual salary statements or other personal data, including in electronic format) and allow access to sites and premises for on-the-spot visits or inspections — as provided for under these Regulations.

To this end, the beneficiary concerned must keep all relevant information relating to the action, at least until the time-limit set out in the Data Sheet (Point 6) and, in any case, until any ongoing checks, reviews, audits, investigations, litigation or other pursuits of claims have been concluded.

25.5 Consequences of checks, reviews, audits and investigations — Extension of results of reviews, audits or investigations

25.5.1 Consequences of checks, reviews, audits and investigations in this grant

Findings in checks, reviews, audits or investigations carried out in the context of this grant may lead to rejections (see Article 27), grant reduction (see Article 28) or other measures described in Chapter 5.

Rejections or grant reductions after the final payment will lead to a revised final grant amount (see Article 22).

Findings in checks, reviews, audits or investigations during the action implementation may lead to a request for amendment (see Article 39), to change the description of the action set out in Annex 1.

Checks, reviews, audits or investigations that find systemic or recurrent errors, irregularities, fraud

[19] Regulation (EU, Euratom) No 883/2013 of the European Parliament and of the Council of 11 September 2013 concerning investigations conducted by the European Anti-Fraud Office (OLAF) and repealing Regulation (EC) No 1073/1999 of the European Parliament and of the Council and Council Regulation (Euratom) No 1074/1999 (OJ L 248, 18/09/2013, p. 1).

[20] Council Regulation (Euratom, EC) No 2185/96 of 11 November 1996 concerning on-the-spot checks and inspections carried out by the Commission in order to protect the European Communities' financial interests against fraud and other irregularities (OJ L 292, 15/11/1996, p. 2).

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or breach of obligations in any EU grant may also lead to consequences in other EU grants awarded under similar conditions ('extension to other grants').

Moreover, findings arising from an OLAF or EPPO investigation may lead to criminal prosecution under national law.

25.5.2 Extension from other grants

Results of checks, reviews, audits or investigations in other grants may be extended to this grant, if:

(a) the beneficiary concerned is found, in other EU grants awarded under similar conditions, to have committed systemic or recurrent errors, irregularities, fraud or breach of obligations that have a material impact on this grant and

(b) those findings are formally notified to the beneficiary concerned — together with the list of grants affected by the findings — within the time-limit for audits set out in the Data Sheet (see Point 6).

The granting authority will formally notify the beneficiary concerned of the intention to extend the findings and the list of grants affected.

If the extension concerns **rejections of costs or contributions**: the notification will include:

(a) an invitation to submit observations on the list of grants affected by the findings

(b) the request to submit revised financial statements for all grants affected

(c) the correction rate for extrapolation, established on the basis of the systemic or recurrent errors, to calculate the amounts to be rejected, if the beneficiary concerned:

(i) considers that the submission of revised financial statements is not possible or practicable or

(ii) does not submit revised financial statements.

If the extension concerns **grant reductions**: the notification will include:

(a) an invitation to submit observations on the list of grants affected by the findings and

(b) the **correction rate for extrapolation**, established on the basis of the systemic or recurrent errors and the principle of proportionality.

The beneficiary concerned has **60 days** from receiving notification to submit observations, revised financial statements or to propose a duly substantiated **alternative correction method/rate**.

On the basis of this, the granting authority will analyse the impact and decide on the implementation (i.e. start rejection or grant reduction procedures, either on the basis of the revised financial statements or the announced/alternative method/rate or a mix of those; see Articles 27 and 28).

25.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, costs or contributions insufficiently

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substantiated will be ineligible (see Article 6) and will be rejected (see Article 27), and the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 26 — IMPACT EVALUATIONS

26.1 Impact evaluation

The granting authority may carry out impact evaluations of the action, measured against the objectives and indicators of the EU programme funding the grant.

Such evaluations may be started during implementation of the action and until the time-limit set out in the Data Sheet (see Point 6). They will be formally notified to the coordinator or beneficiaries and will be considered to start on the date of the notification.

If needed, the granting authority may be assisted by independent outside experts.

The coordinator or beneficiaries must provide any information relevant to evaluate the impact of the action, including information in electronic format.

26.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the granting authority may apply the measures described in Chapter 5.

CHAPTER 5 CONSEQUENCES OF NON-COMPLIANCE

SECTION 1 REJECTIONS AND GRANT REDUCTION

ARTICLE 27 — REJECTION OF COSTS AND CONTRIBUTIONS

27.1 Conditions

The granting authority will — at beneficiary termination, interim payment, final payment or afterwards — reject any costs or contributions which are ineligible (see Article 6), in particular following checks, reviews, audits or investigations (see Article 25).

The rejection may also be based on the extension of findings from other grants to this grant (see Article 25).

Ineligible costs or contributions will be rejected.

27.2 Procedure

If the rejection does not lead to a recovery, the granting authority will formally notify the coordinator or beneficiary concerned of the rejection, the amounts and the reasons why. The coordinator or beneficiary concerned may — within 30 days of receiving notification — submit observations if it disagrees with the rejection (payment review procedure).

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If the rejection leads to a recovery, the granting authority will follow the contradictory procedure with pre-information letter set out in Article 22.

27.3 Effects

If the granting authority rejects costs or contributions, it will deduct them from the costs or contributions declared and then calculate the amount due (and, if needed, make a recovery; see Article 22).

ARTICLE 28 — GRANT REDUCTION

28.1 Conditions

The granting authority may — at beneficiary termination, final payment or afterwards — reduce the grant for a beneficiary, if:

(a) the beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.), or

(b) the beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (see Article 25).

The amount of the reduction will be calculated for each beneficiary concerned and proportionate to the seriousness and the duration of the errors, irregularities or fraud or breach of obligations, by applying an individual reduction rate to their accepted EU contribution.

28.2 Procedure

If the grant reduction does not lead to a recovery, the granting authority will formally notify the coordinator or beneficiary concerned of the reduction, the amount to be reduced and the reasons why. The coordinator or beneficiary concerned may — within 30 days of receiving notification — submit observations if it disagrees with the reduction (payment review procedure).

If the grant reduction leads to a recovery, the granting authority will follow the contradictory procedure with pre-information letter set out in Article 22.

28.3 Effects

If the granting authority reduces the grant, it will deduct the reduction and then calculate the amount due (and, if needed, make a recovery; see Article 22).

SECTION 2 SUSPENSION AND TERMINATION

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ARTICLE 29 — PAYMENT DEADLINE SUSPENSION

29.1 Conditions

The granting authority may — at any moment — suspend the payment deadline if a payment cannot be processed because:

(a) the required report (see Article 21) has not been submitted or is not complete or additional information is needed

(b) there are doubts about the amount to be paid (e.g. ongoing audit extension procedure, queries about eligibility, need for a grant reduction, etc.) and additional checks, reviews, audits or investigations are necessary, or

(c) there are other issues affecting the EU financial interests.

29.2 Procedure

The granting authority will formally notify the coordinator of the suspension and the reasons why.

The suspension will **take effect** the day the notification is sent.

If the conditions for suspending the payment deadline are no longer met, the suspension will be **lifted** — and the remaining time to pay (see Data Sheet, Point 4.2) will resume.

If the suspension exceeds two months, the coordinator may request the granting authority to confirm if the suspension will continue.

If the payment deadline has been suspended due to the non-compliance of the report and the revised report is not submitted (or was submitted but is also rejected), the granting authority may also terminate the grant or the participation of the coordinator (see Article 32).

ARTICLE 30 — PAYMENT SUSPENSION

30.1 Conditions

The granting authority may — at any moment — suspend payments, in whole or in part for one or more beneficiaries, if:

(a) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed or is suspected of having committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.), or

(b) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants

awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant.

If payments are suspended for one or more beneficiaries, the granting authority will make partial payment(s) for the part(s) not suspended. If suspension concerns the final payment, the payment (or recovery) of the remaining amount after suspension is lifted will be considered to be the payment that closes the action.

30.2 Procedure

Before suspending payments, the granting authority will send a **pre-information letter** to the beneficiary concerned:

- formally notifying the intention to suspend payments and the reasons why and
- requesting observations within 30 days of receiving notification.

If the granting authority does not receive observations or decides to pursue the procedure despite the observations it has received, it will confirm the suspension (**confirmation letter**). Otherwise, it will formally notify that the procedure is discontinued.

At the end of the suspension procedure, the granting authority will also inform the coordinator.

The suspension will **take effect** the day after the confirmation notification is sent.

If the conditions for resuming payments are met, the suspension will be **lifted**. The granting authority will formally notify the beneficiary concerned (and the coordinator) and set the suspension end date.

During the suspension, no prefinancing will be paid to the beneficiaries concerned. For interim payments, the periodic reports for all reporting periods except the last one (see Article 21) must not contain any financial statements from the beneficiary concerned (or its affiliated entities). The coordinator must include them in the next periodic report after the suspension is lifted or — if suspension is not lifted before the end of the action — in the last periodic report.

ARTICLE 31 — GRANT AGREEMENT SUSPENSION

31.1 Consortium-requested GA suspension

31.1.1 Conditions and procedure

The beneficiaries may request the suspension of the grant or any part of it, if exceptional circumstances — in particular *force majeure* (see Article 35) — make implementation impossible or excessively difficult.

The coordinator must submit a request for **amendment** (see Article 39), with:

- the reasons why
- the date the suspension takes effect; this date may be before the date of the submission of the amendment request and
- the expected date of resumption.

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The suspension will **take effect** on the day specified in the amendment.

Once circumstances allow for implementation to resume, the coordinator must immediately request another **amendment** of the Agreement to set the suspension end date, the resumption date (one day after suspension end date), extend the duration and make other changes necessary to adapt the action to the new situation (see Article 39) — unless the grant has been terminated (see Article 32). The suspension will be **lifted** with effect from the suspension end date set out in the amendment. This date may be before the date of the submission of the amendment request.

During the suspension, no prefinancing will be paid. Costs incurred or contributions for activities implemented during grant suspension are not eligible (see Article 6.3).

31.2 EU-initiated GA suspension

31.2.1 Conditions

The granting authority may suspend the grant or any part of it, if:

(a) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed or is suspected of having committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.), or

(b) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant

(c) other:

  (i) linked action issues: not applicable

  (ii) the action has lost its scientific or technological relevance, for EIC Accelerator actions: the action has lost its economic relevance, for challenge-based EIC Pathfinder actions and Horizon Europe Missions: the action has lost its relevance as part of the Portfolio for which it has been initially selected

31.2.2 Procedure

Before suspending the grant, the granting authority will send a **pre-information letter** to the coordinator:

- formally notifying the intention to suspend the grant and the reasons why and
- requesting observations within 30 days of receiving notification.

If the granting authority does not receive observations or decides to pursue the procedure despite the

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observations it has received, it will confirm the suspension (**confirmation letter**). Otherwise, it will formally notify that the procedure is discontinued.

The suspension will **take effect** the day after the confirmation notification is sent (or on a later date specified in the notification).

Once the conditions for resuming implementation of the action are met, the granting authority will formally notify the coordinator a **lifting of suspension letter**, in which it will set the suspension end date and invite the coordinator to request an amendment of the Agreement to set the resumption date (one day after suspension end date), extend the duration and make other changes necessary to adapt the action to the new situation (see Article 39) — unless the grant has been terminated (see Article 32). The suspension will be **lifted** with effect from the suspension end date set out in the lifting of suspension letter. This date may be before the date on which the letter is sent.

During the suspension, no prefinancing will be paid. Costs incurred or contributions for activities implemented during suspension are not eligible (see Article 6.3).

The beneficiaries may not claim damages due to suspension by the granting authority (see Article 33).

Grant suspension does not affect the granting authority's right to terminate the grant or a beneficiary (see Article 32) or reduce the grant (see Article 28).

ARTICLE 32 — GRANT AGREEMENT OR BENEFICIARY TERMINATION

32.1 Consortium-requested GA termination

32.1.1 Conditions and procedure

The beneficiaries may request the termination of the grant.

The coordinator must submit a request for **amendment** (see Article 39), with:

- the reasons why
- the date the consortium ends work on the action ('end of work date') and
- the date the termination takes effect ('termination date'); this date must be after the date of the submission of the amendment request.

The termination will **take effect** on the termination date specified in the amendment.

If no reasons are given or if the granting authority considers the reasons do not justify termination, it may consider the grant terminated improperly.

32.1.2 Effects

The coordinator must — within 60 days from when termination takes effect — submit a **periodic report** (for the open reporting period until termination).

The granting authority will calculate the final grant amount and final payment on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented

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before the end of work date (see Article 22). Costs relating to contracts due for execution only after the end of work are not eligible.

If the granting authority does not receive the report within the deadline, only costs and contributions which are included in an approved periodic report will be taken into account (no costs/contributions if no periodic report was ever approved).

Improper termination may lead to a grant reduction (see Article 28).

After termination, the beneficiaries' obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

32.2 Consortium-requested beneficiary termination

32.2.1 Conditions and procedure

The coordinator may request the termination of the participation of one or more beneficiaries, on request of the beneficiary concerned or on behalf of the other beneficiaries.

The coordinator must submit a request for **amendment** (see Article 39), with:

- the reasons why
- the opinion of the beneficiary concerned (or proof that this opinion has been requested in writing)
- the date the beneficiary ends work on the action ('end of work date')
- the date the termination takes effect ('termination date'); this date must be after the date of the submission of the amendment request.

If the termination concerns the coordinator and is done without its agreement, the amendment request must be submitted by another beneficiary (acting on behalf of the consortium).

The termination will **take effect** on the termination date specified in the amendment.

If no information is given or if the granting authority considers that the reasons do not justify termination, it may consider the beneficiary to have been terminated improperly.

32.2.2 Effects

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a **report on the distribution of payments** to the beneficiary concerned

(ii) a **termination report** from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, the financial statement, the explanation on the use of resources, and, if applicable, the certificate on the financial statement (CFS; see Articles 21 and 24.2 and Data Sheet, Point 4.3)

(iii) a second **request for amendment** (see Article 39) with other amendments needed (e.g.

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reallocation of the tasks and the estimated budget of the terminated beneficiary; addition of a new beneficiary to replace the terminated beneficiary; change of coordinator, etc.).

The granting authority will calculate the amount due to the beneficiary on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before the end of work date (see Article 22). Costs relating to contracts due for execution only after the end of work are not eligible.

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 21).

If the granting authority does not receive the termination report within the deadline, only costs and contributions which are included in an approved periodic report will be taken into account (no costs/ contributions if no periodic report was ever approved).

If the granting authority does not receive the report on the distribution of payments within the deadline, it will consider that:

- the coordinator did not distribute any payment to the beneficiary concerned and that
- the beneficiary concerned must not repay any amount to the coordinator.

If the second request for amendment is accepted by the granting authority, the Agreement is **amended** to introduce the necessary changes (see Article 39).

If the second request for amendment is rejected by the granting authority (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the grant may be terminated (see Article 32).

Improper termination may lead to a reduction of the grant (see Article 31) or grant termination (see Article 32).

After termination, the concerned beneficiary's obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

32.3 EU-initiated GA or beneficiary termination

32.3.1 Conditions

The granting authority may terminate the grant or the participation of one or more beneficiaries, if:

(a) one or more beneficiaries do not accede to the Agreement (see Article 40)

(b) a change to the action or the legal, financial, technical, organisational or ownership situation of a beneficiary is likely to substantially affect the implementation of the action or calls into question the decision to award the grant (including changes linked to one of the exclusion grounds listed in the declaration of honour)

(c) following termination of one or more beneficiaries, the necessary changes to the Agreement

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(and their impact on the action) would call into question the decision awarding the grant or breach the principle of equal treatment of applicants

(d) implementation of the action has become impossible or the changes necessary for its continuation would call into question the decision awarding the grant or breach the principle of equal treatment of applicants

(e) a beneficiary (or person with unlimited liability for its debts) is subject to bankruptcy proceedings or similar (including insolvency, winding-up, administration by a liquidator or court, arrangement with creditors, suspension of business activities, etc.)

(f) a beneficiary (or person with unlimited liability for its debts) is in breach of social security or tax obligations

(g) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has been found guilty of grave professional misconduct

(h) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed fraud, corruption, or is involved in a criminal organisation, money laundering, terrorism-related crimes (including terrorism financing), child labour or human trafficking

(i) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) was created under a different jurisdiction with the intent to circumvent fiscal, social or other legal obligations in the country of origin (or created another entity with this purpose)

(j) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.)

(k) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (extension of findings from other grants to this grant; see Article 25)

(l) despite a specific request by the granting authority, a beneficiary does not request — through the coordinator — an amendment to the Agreement to end the participation of one of its affiliated entities or associated partners that is in one of the situations under points (d), (f), (e), (g), (h), (i) or (j) and to reallocate its tasks, or

(m) other:

  (i) linked action issues: not applicable

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(ii) the action has lost its scientific or technological relevance, for EIC Accelerator actions: the action has lost its economic relevance, for challenge-based EIC Pathfinder actions and Horizon Europe Missions: the action has lost its relevance as part of the Portfolio for which it has been initially selected

32.3.2 Procedure

Before terminating the grant or participation of one or more beneficiaries, the granting authority will send **a pre-information letter** to the coordinator or beneficiary concerned:

- formally notifying the intention to terminate and the reasons why and
- requesting observations within 30 days of receiving notification.

If the granting authority does not receive observations or decides to pursue the procedure despite the observations it has received, it will confirm the termination and the date it will take effect (**confirmation letter**). Otherwise, it will formally notify that the procedure is discontinued.

For beneficiary terminations, the granting authority will — at the end of the procedure — also inform the coordinator.

The termination will **take effect** the day after the confirmation notification is sent (or on a later date specified in the notification; 'termination date').

32.3.3 Effects

(a) for **GA termination**:

The coordinator must — within 60 days from when termination takes effect — submit a **periodic report** (for the last open reporting period until termination).

The granting authority will calculate the final grant amount and final payment on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before termination takes effect (see Article 22). Costs relating to contracts due for execution only after termination are not eligible.

If the grant is terminated for breach of the obligation to submit reports, the coordinator may not submit any report after termination.

If the granting authority does not receive the report within the deadline, only costs and contributions which are included in an approved periodic report will be taken into account (no costs/contributions if no periodic report was ever approved).

Termination does not affect the granting authority's right to reduce the grant (see Article 28) or to impose administrative sanctions (see Article 34).

The beneficiaries may not claim damages due to termination by the granting authority (see Article 33).

After termination, the beneficiaries' obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25

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(checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

(b) for **beneficiary termination**:

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a **report on the distribution of payments** to the beneficiary concerned

(ii) a **termination report** from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, the financial statement, the explanation on the use of resources, and, if applicable, the certificate on the financial statement (CFS; see Articles 21 and 24.2 and Data Sheet, Point 4.3)

(iii) a **request for amendment** (see Article 39) with any amendments needed (e.g. reallocation of the tasks and the estimated budget of the terminated beneficiary; addition of a new beneficiary to replace the terminated beneficiary; change of coordinator, etc.).

The granting authority will calculate the amount due to the beneficiary on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before termination takes effect (see Article 22). Costs relating to contracts due for execution only after termination are not eligible.

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 21).

If the granting authority does not receive the termination report within the deadline, only costs and contributions included in an approved periodic report will be taken into account (no costs/ contributions if no periodic report was ever approved).

If the granting authority does not receive the report on the distribution of payments within the deadline, it will consider that:

- the coordinator did not distribute any payment to the beneficiary concerned and that
- the beneficiary concerned must not repay any amount to the coordinator.

If the request for amendment is accepted by the granting authority, the Agreement is **amended** to introduce the necessary changes (see Article 39).

If the request for amendment is rejected by the granting authority (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the grant may be terminated (see Article 32).

After termination, the concerned beneficiary's obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

SECTION 3 OTHER CONSEQUENCES: DAMAGES AND ADMINISTRATIVE SANCTIONS

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ARTICLE 33 — DAMAGES

33.1 Liability of the granting authority

The granting authority cannot be held liable for any damage caused to the beneficiaries or to third parties as a consequence of the implementation of the Agreement, including for gross negligence.

The granting authority cannot be held liable for any damage caused by any of the beneficiaries or other participants involved in the action, as a consequence of the implementation of the Agreement.

33.2 Liability of the beneficiaries

The beneficiaries must compensate the granting authority for any damage it sustains as a result of the implementation of the action or because the action was not implemented in full compliance with the Agreement, provided that it was caused by gross negligence or wilful act.

The liability does not extend to indirect or consequential losses or similar damage (such as loss of profit, loss of revenue or loss of contracts), provided such damage was not caused by wilful act or by a breach of confidentiality.

ARTICLE 34 — ADMINISTRATIVE SANCTIONS AND OTHER MEASURES

Nothing in this Agreement may be construed as preventing the adoption of administrative sanctions (i.e. exclusion from EU award procedures and/or financial penalties) or other public law measures, in addition or as an alternative to the contractual measures provided under this Agreement (see, for instance, Articles 135 to 145 EU Financial Regulation 2018/1046 and Articles 4 and 7 of Regulation 2988/95[21]).

SECTION 4 FORCE MAJEURE

ARTICLE 35 — FORCE MAJEURE

A party prevented by force majeure from fulfilling its obligations under the Agreement cannot be considered in breach of them.

‘Force majeure’ means any situation or event that:

- prevents either party from fulfilling their obligations under the Agreement,
- was unforeseeable, exceptional situation and beyond the parties’ control,
- was not due to error or negligence on their part (or on the part of other participants involved in the action), and
- proves to be inevitable in spite of exercising all due diligence.

Any situation constituting force majeure must be formally notified to the other party without delay, stating the nature, likely duration and foreseeable effects.

[21] Council Regulation (EC, Euratom) No 2988/95 of 18 December 1995 on the protection of the European Communities financial interests (OJ L 312, 23.12.1995, p. 1).

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The parties must immediately take all the necessary steps to limit any damage due to force majeure and do their best to resume implementation of the action as soon as possible.

CHAPTER 6 FINAL PROVISIONS

ARTICLE 36 — COMMUNICATION BETWEEN THE PARTIES

36.1 Forms and means of communication — Electronic management

EU grants are managed fully electronically through the EU Funding & Tenders Portal ('Portal').

All communications must be made electronically through the Portal, in accordance with the Portal Terms and Conditions and using the forms and templates provided there (except if explicitly instructed otherwise by the granting authority).

Communications must be made in writing and clearly identify the grant agreement (project number and acronym).

Communications must be made by persons authorised according to the Portal Terms and Conditions. For naming the authorised persons, each beneficiary must have designated — before the signature of this Agreement — a 'legal entity appointed representative (LEAR)'. The role and tasks of the LEAR are stipulated in their appointment letter (see Portal Terms and Conditions).

If the electronic exchange system is temporarily unavailable, instructions will be given on the Portal.

36.2 Date of communication

The sending date for communications made through the Portal will be the date and time of sending, as indicated by the time logs.

The receiving date for communications made through the Portal will be the date and time the communication is accessed, as indicated by the time logs. Formal notifications that have not been accessed within 10 days after sending, will be considered to have been accessed (see Portal Terms and Conditions).

If a communication is exceptionally made on paper (by e-mail or postal service), general principles apply (i.e. date of sending/receipt). Formal notifications by registered post with proof of delivery will be considered to have been received either on the delivery date registered by the postal service or the deadline for collection at the post office.

If the electronic exchange system is temporarily unavailable, the sending party cannot be considered in breach of its obligation to send a communication within a specified deadline.

36.3 Addresses for communication

The Portal can be accessed via the Europa website.

The address for paper communications to the granting authority (if exceptionally allowed) is the official mailing address indicated on its website.

For beneficiaries, it is the legal address specified in the Portal Participant Register.

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ARTICLE 37 — INTERPRETATION OF THE AGREEMENT

The provisions in the Data Sheet take precedence over the rest of the Terms and Conditions of the Agreement.

Annex 5 takes precedence over the Terms and Conditions; the Terms and Conditions take precedence over the Annexes other than Annex 5.

Annex 2 takes precedence over Annex 1.

ARTICLE 38 — CALCULATION OF PERIODS AND DEADLINES

In accordance with Regulation No 1182/71[22], periods expressed in days, months or years are calculated from the moment the triggering event occurs.

The day during which that event occurs is not considered as falling within the period.

'Days' means calendar days, not working days.

ARTICLE 39 — AMENDMENTS

39.1 Conditions

The Agreement may be amended, unless the amendment entails changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

Amendments may be requested by any of the parties.

39.2 Procedure

The party requesting an amendment must submit a request for amendment signed directly in the Portal Amendment tool.

The coordinator submits and receives requests for amendment on behalf of the beneficiaries (see Annex 3). If a change of coordinator is requested without its agreement, the submission must be done by another beneficiary (acting on behalf of the other beneficiaries).

The request for amendment must include:

- the reasons why
- the appropriate supporting documents and
- for a change of coordinator without its agreement: the opinion of the coordinator (or proof that this opinion has been requested in writing).

The granting authority may request additional information.

[22] Regulation (EEC, Euratom) No 1182/71 of the Council of 3 June 1971 determining the rules applicable to periods, dates and time-limits (OJ L 124, 8/6/1971, p. 1).

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If the party receiving the request agrees, it must sign the amendment in the tool within 45 days of receiving notification (or any additional information the granting authority has requested). If it does not agree, it must formally notify its disagreement within the same deadline. The deadline may be extended, if necessary for the assessment of the request. If no notification is received within the deadline, the request is considered to have been rejected.

An amendment **enters into force** on the day of the signature of the receiving party.

An amendment **takes effect** on the date of entry into force or other date specified in the amendment.

ARTICLE 40 — ACCESSION AND ADDITION OF NEW BENEFICIARIES

40.1 Accession of the beneficiaries mentioned in the Preamble

The beneficiaries which are not coordinator must accede to the grant by signing the accession form (see Annex 3) directly in the Portal Grant Preparation tool, within 30 days after the entry into force of the Agreement (see Article 44).

They will assume the rights and obligations under the Agreement with effect from the date of its entry into force (see Article 44).

If a beneficiary does not accede to the grant within the above deadline, the coordinator must — within 30 days — request an amendment (see Article 39) to terminate the beneficiary and make any changes necessary to ensure proper implementation of the action. This does not affect the granting authority's right to terminate the grant (see Article 32).

40.2 Addition of new beneficiaries

In justified cases, the beneficiaries may request the addition of a new beneficiary.

For this purpose, the coordinator must submit a request for amendment in accordance with Article 39. It must include an accession form (see Annex 3) signed by the new beneficiary directly in the Portal Amendment tool.

New beneficiaries will assume the rights and obligations under the Agreement with effect from the date of their accession specified in the accession form (see Annex 3).

Additions are also possible in mono-beneficiary grants.

ARTICLE 41 — TRANSFER OF THE AGREEMENT

In justified cases, the beneficiary of a mono-beneficiary grant may request the transfer of the grant to a new beneficiary, provided that this would not call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

The beneficiary must submit a request for **amendment** (see Article 39), with

- the reasons why
- the accession form (see Annex 3) signed by the new beneficiary directly in the Portal Amendment tool and

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- additional supporting documents (if required by the granting authority).

The new beneficiary will assume the rights and obligations under the Agreement with effect from the date of accession specified in the accession form (see Annex 3).

ARTICLE 42 — ASSIGNMENTS OF CLAIMS FOR PAYMENT AGAINST THE GRANTING AUTHORITY

The beneficiaries may not assign any of their claims for payment against the granting authority to any third party, except if expressly approved in writing by the granting authority on the basis of a reasoned, written request by the coordinator (on behalf of the beneficiary concerned).

If the granting authority has not accepted the assignment or if the terms of it are not observed, the assignment will have no effect on it.

In no circumstances will an assignment release the beneficiaries from their obligations towards the granting authority.

ARTICLE 43 — APPLICABLE LAW AND SETTLEMENT OF DISPUTES

43.1 Applicable law

The Agreement is governed by the applicable EU law, supplemented if necessary by the law of Belgium.

Special rules may apply for beneficiaries which are international organisations (if any; see Data Sheet, Point 5).

43.2 Dispute settlement

If a dispute concerns the interpretation, application or validity of the Agreement, the parties must bring action before the EU General Court — or, on appeal, the EU Court of Justice — under Article 272 of the Treaty on the Functioning of the EU (TFEU).

For non-EU beneficiaries (if any), such disputes must be brought before the courts of Brussels, Belgium — unless an international agreement provides for the enforceability of EU court judgements.

For beneficiaries with arbitration as special dispute settlement forum (if any; see Data Sheet, Point 5), the dispute will — in the absence of an amicable settlement — be settled in accordance with the Rules for Arbitration published on the Portal.

If a dispute concerns administrative sanctions, offsetting or an enforceable decision under Article 299 TFEU (see Articles 22 and 34), the beneficiaries must bring action before the General Court — or, on appeal, the Court of Justice — under Article 263 TFEU.

For grants where the granting authority is an EU executive agency (see Preamble), actions against offsetting and enforceable decisions must be brought against the European Commission (not against the granting authority; see also Article 22).

ARTICLE 44 — ENTRY INTO FORCE

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The Agreement will enter into force on the day of signature by the granting authority or the coordinator, depending on which is later.

SIGNATURES

For the coordinator

For the granting authority

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ANNEX 1



Horizon Europe (HORIZON)

Description of the action (DoA)

Part A

Part B

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DESCRIPTION OF THE ACTION (PART A)

COVER PAGE

Part A of the Description of the Action (DoA) must be completed directly on the Portal Grant Preparation screens.

PROJECT *Grant Preparation (General Information screen) — Enter the info.*	
Project number:	101156595
Project name:	EUROPEAN RARE DISEASES RESEARCH ALLIANCE
Project acronym:	ERDERA
Call:	HORIZON-HLTH-2023-DISEASE-07
Topic:	HORIZON-HLTH-2023-DISEASE-07-01
Type of action:	HORIZON-COFUND
Service:	HADEA/A/03
Project starting date:	fixed date: 1 September 2024
Project duration:	84 months

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List of critical risks 118
Project reviews 124

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PROJECT SUMMARY

Project summary

Grant Preparation (General Information screen) — Provide an overall description of your project (including context and overall objectives, planned activities and main achievements, and expected results and impacts (on target groups, change procedures, capacities, innovation etc)). This summary should give readers a clear idea of what your project is about.

Use the project summary from your proposal.

The European Rare Diseases Research Alliance (ERDERA) aims to improve the health and well-being of the 30 million people living with a rare disease in Europe, by making Europe a world leader in Rare Disease (RD) research and innovation, to support concrete health benefits to rare disease patients, through better prevention, diagnosis and treatment. This Partnership will deliver a RD ecosystem that builds on the successes of previous programmes by supporting robust patient need-led research, developing new diagnostic methods and pathways, spearheading the digital transformational change connecting the dots between care, patient data and research, while ensuring strong alignment of strategies in RD research across countries and regions. Structuring goal-oriented public-private collaborations targeted at interventions all along the R&D value chain will ensure that the journey from knowledge to patient impact is expedited, thereby optimising EU innovation potential in RD. To support its ambition and missions ERDERA has been designed as a comprehensive and integrated ecosystem of which structure can be compared to an institute encompassing three main parts: (i) funding, (ii) internal (in house) Clinical Research Network that implements research activities targeting clinical trial readiness of RDs and accelerating diagnosis and translation of research discovery into improved patient care, and (iii) related supporting services (Data, Expertise, Education and Training) as well as an acceleration hub that serve external and internal RD community, all supported by all-embracing coordination and strategy and foundational (inter)national alignment.

LIST OF PARTICIPANTS

PARTICIPANTS

Grant Preparation (Beneficiaries screen) — Enter the info.

Number	Role	Short name	Legal name	Country	PIC
1	COO	INSERM	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE	FR	999997833
1.1	AE	CAD	Collecteur Analyseur de Données	FR	880793078
2	BEN	TEAMIT	TEAMIT RESEARCH SL	ES	896104237
3	BEN	DLR	DEUTSCHES ZENTRUM FUR LUFT - UND RAUMFAHRT EV	DE	999981731
4	BEN	ANR	AGENCE NATIONALE DE LA RECHERCHE	FR	998711613
5	BEN	FTELE	FONDAZIONE TELETHON ETS	IT	999448716
6	BEN	LMT	Lietuvos mokslo taryba	LT	997808446
7	BEN	ZonMw	ZORGONDERZOEK NEDERLAND ZON	NL	999544164
8	BEN	UT	EBERHARD KARLS UNIVERSITAET TUEBINGEN	DE	999991916
9	BEN	UTARTU	TARTU ULIKOOL	EE	999895013
10	BEN	CNAG	CONSORCIO PARA LA EXPLOTACION DEL CENTRO NACIONAL DE ANALISIS GENOMICO	ES	882802433

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PARTICIPANTS

Grant Preparation (Beneficiaries screen) — Enter the info.

Number	Role	Short name	Legal name	Country	PIC
11	BEN	SRUMC	STICHTING RADBOUD UNIVERSITAIR MEDISCH CENTRUM	NL	892057785
12	BEN	TUM	TECHNISCHE UNIVERSITAET MUENCHEN	DE	999977463
13	BEN	UKHD	UNIVERSITATSKLINIKUM HEIDELBERG	DE	999841081
14	BEN	C-PATH	CRITICAL PATH INSTITUTE STICHTING	NL	887895418
15	BEN	VHIR	FUNDACIO HOSPITAL UNIVERSITARI VALL D'HEBRON - INSTITUT DE RECERCA	ES	999541642
16	BEN	LUMC	ACADEMISCH ZIEKENHUIS LEIDEN	NL	999990849
17	BEN	UTWENTE	UNIVERSITEIT TWENTE	NL	999900833
18	BEN	UPM	UNIVERSIDAD POLITECNICA DE MADRID	ES	999974844
19	BEN	UMCG	ACADEMISCH ZIEKENHUIS GRONINGEN	NL	999914801
20	BEN	AUMC	STICHTING AMSTERDAM UMC	NL	919322739
21	BEN	UM	UNIVERSITEIT MAASTRICHT	NL	999975911
22	BEN	EATRIS	EATRIS ERIC	NL	941506445
23	BEN	FGB	FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS	IT	962478330
24	BEN	APHP	ASSISTANCE PUBLIQUE HOPITAUX DE PARIS	FR	999645432
25	BEN	UHASSELT	UNIVERSITEIT HASSELT	BE	999874934
26	BEN	EURORDIS	EURORDIS - RARE DISEASES EUROPE	FR	965288323
27	BEN	VULSK	VIESOJI ISTAIGA VILNIAUS UNIVERSITETO LIGONINE SANTAROS KLINIKOS	LT	991636530
28	BEN	UC	UNIVERSIDADE DE COIMBRA	PT	997826391
29	BEN	FFRD	FONDATION MALADIES RARES	FR	954438485
30	BEN	AFM	ASS FRANCAISE CONTRE LES MYOPATHIES	FR	959828387
31	BEN	CCUH	BERNU KLINISKA UNIVERSITATES SLIMNICA VALSTS SIA	LV	904374748
32	BEN	AICIB	AICIB - AGENCIA DE INVESTIGACAO CLINICA E INOVACAO BIOMEDICA	PT	892687606
33	BEN	IMGGE	INSTITUT ZA MOLEKULARNU GENETIKU I GENETICKO INZENJERSTVO	RS	986427921
34	BEN	RDI	RARE DISEASES INTERNATIONAL	FR	881348694
35	BEN	ACU	ACIBADEM MEHMET ALI AYDINLAR UNIVERSITY	TR	959704421
36	BEN	AIT	AIT AUSTRIAN INSTITUTE OF TECHNOLOGY GMBH	AT	999584128
37	BEN	AMU	UNIVERSITE D'AIX MARSEILLE	FR	955518483
38	BEN	AOU Meyer IRCCS	AZIENDA OSPEDALIERA UNIVERSITARIA MEYER IRCCS	IT	998778543

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PARTICIPANTS

Grant Preparation (Beneficiaries screen) — Enter the info.

Number	Role	Short name	Legal name	Country	PIC
39	BEN	ASU-FC	AZIENDA SANITARIA UNIVERSITARIA FRIULI CENTRALE	IT	894464355
40	BEN	BIU	BAR ILAN UNIVERSITY	IL	999886574
41	BEN	BMBF	BUNDESMINISTERIUM FUER BILDUNG UND FORSCHUNG	DE	999835455
42	BEN	CCRI GmbH	ST. ANNA KINDERKREBSFORSCHUNG GMBH	AT	891384896
43	BEN	CENTOGENE	CENTOGENE GMBH	DE	878333449
44	BEN	CHARITE	CHARITE - UNIVERSITAETSMEDIZIN BERLIN	DE	999992692
45	BEN	CHI	CHECKIMMUNE GMBH	DE	889852781
46	BEN	CHU Dijon	CENTRE HOSPITALIER REG UNIVERSITAIRE DIJON	FR	959994451
47	BEN	CE	COPENHAGEN ECONOMICS AS	DK	938801309
48	BEN	REGIONH	REGION HOVEDSTADEN	DK	999654744
49	BEN	CSO-MOH	MINISTRY OF HEALTH	IL	999596156
50	BEN	CVBF	CONSORZIO PER VALUTAZIONI BIOLOGICHE E FARMACOLOGICHE	IT	999717018
51	BEN	DDF	STICHTING DUCHENNE DATA FOUNDATION	NL	899914882
52	BEN	ELS	ELSEVIER BV	NL	999937014
53	BEN	Erasmus MC	ERASMUS UNIVERSITAIR MEDISCH CENTRUM ROTTERDAM	NL	999988424
54	BEN	F.R.S.-FNRS	FONDS DE LA RECHERCHE SCIENTIFIQUE-FNRS	BE	999540381
55	BEN	FHG	FRAUNHOFER GESELLSCHAFT ZUR FORDERUNG DER ANGEWANDTEN FORSCHUNG EV	DE	999984059
56	BEN	FRRB	FONDAZIONE REGIONALE PER LA RICERCA BIOMEDICA	IT	929009450
57	BEN	ECRIN	ECRIN EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK	FR	948646712
58	BEN	FWF	FONDS ZUR FÖRDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG	AT	998735960
59	BEN	IFD	INNOVATIONSFONDEN	DK	939076692
60	BEN	FSJD-CERCA	FUNDACIO PRIVADA PER A LA RECERCA I LA DOCENCIA SANT JOAN DE DEU	ES	999565601
61	BEN	FCT	FUNDACAO PARA A CIENCIA E A TECNOLOGIA	PT	999543970
62	BEN	MZd	MINISTERSTVO ZDRAVOTNICTVI CESKE REPUBLIKY	CZ	924144512
62.1	AE	AZV	AGENTURA PRO ZDRAVOTNICKY VYZKUM CESKE REPUBLIKY AZV CR	CZ	878890229

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PARTICIPANTS

Grant Preparation (Beneficiaries screen) — Enter the info.

Number	Role	Short name	Legal name	Country	PIC
63	BEN	GNT	ASSOCIATION GENETHON	FR	998217883
64	BEN	GERAD	GEORGIAN FOUNDATION FOR GENETIC AND RARE DISEASES	GE	953089312
65	BEN	RS	REGION STOCKHOLM	SE	999522921
66	BEN	GUF	JOHANN WOLFGANG GOETHE-UNIVERSITAET FRANKFURT AM MAIN	DE	999978724
67	BEN	HRB	THE HEALTH RESEARCH BOARD	IE	999546686
68	BEN	İBG	IZMIR BIYOTIP VE GENOM MERKEZI	TR	906758620
69	BEN	Rannis	RANNSOKNAMIDSTOD ISLANDS	IS	999547268
70	BEN	IMAGINE	IMAGINE INSTITUT DES MALADIES GENETIQUES NECKER ENFANTS MALADES FONDATION	FR	955276177
71	BEN	IGC PAN	INSTYTUT GENETYKI CZLOWIEKA POLSKIEJ AKADEMII NAUK	PL	982958425
72	BEN	ISCIII	INSTITUTO DE SALUD CARLOS III	ES	999507886
73	BEN	INSA	INSTITUTO NACIONAL DE SAUDE DR. RICARDO JORGE	PT	998308190
74	BEN	IOR	ISTITUTO ORTOPEDICO RIZZOLI	IT	999445709
75	BEN	ISS	ISTITUTO SUPERIORE DI SANITA	IT	999978821
76	BEN	IT-MOH	MINISTERO DELLA SALUTE	IT	999531942
77	BEN	KU Leuven	KATHOLIEKE UNIVERSITEIT LEUVEN	BE	999991334
78	BEN	LZP	LATVIJAS ZINATNES PADOME	LV	999546589
79	BEN	MRT	MAPI RESEARCH TRUST	FR	925695542
80	BEN	MUS	MEDICAL UNIVERSITY SOFIA	BG	999857571
81	BEN	MUH	FAKULTNI NEMOCNICE V MOTOLE	CZ	964458391
82	BEN	MUR	Ministero dell'università e della ricerca	IT	894763406
83	BEN	NCBR	NARODOWE CENTRUM BADAN I ROZWOJU	PL	999519720
84	BEN	NKUA	ETHNIKO KAI KAPODISTRIAKO PANEPISTIMIO ATHINON	EL	999643007
85	BEN	MoH SR	MINISTERSTVO ZDRAVOTNICTVA SLOVENSKEJ REPUBLIKY	SK	999825173
86	BEN	RDG	ENOSI SPANION ASTHENON ELLADOS	EL	883276763
87	BEN	REGIONSYD	REGION SYDDANMARK	DK	999602073
88	BEN	OPBG	OSPEDALE PEDIATRICO BAMBINO GESU	IT	998837810
89	BEN	OSR	OSPEDALE SAN RAFFAELE SRL	IT	953176030
90	BEN	JSI	INSTITUT JOZEF STEFAN	SI	999971837
91	BEN	RCN	NORGES FORSKNINGSRAD	NO	999460453

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Number	Role	Short name	Legal name	Country	PIC
92	BEN	FWO	FONDS VOOR WETENSCHAPPELIJK ONDERZOEK-VLAANDEREN	BE	997949484
93	BEN	REUH	RIGAS AUSTRUMU KLINISKA UNIVERSITATES SLIMNICA SIA	LV	973366483
94	BEN	RIF	IDRYMA EREVNAS KAI KAINOTOMIAS	CY	999946035
95	BEN	RCSI	ROYAL COLLEGE OF SURGEONS IN IRELAND	IE	999867368
96	BEN	RSU	RIGAS STRADINA UNIVERSITATE	LV	999843118
97	BEN	Sciensano	SCIENSANO	BE	906160809
98	BEN	SPW	SERVICE PUBLIC DE WALLONIE	BE	999811884
99	BEN	SFU	SIGMUND FREUD PRIVATUNIVERSITAT WIEN GMBH	AT	996709824
100	BEN	ETAg	SIHTASUTUS EESTI TEADUSAGENTUUR	EE	998483760
101	BEN	SAS	SLOVENSKA AKADEMIA VIED	SK	999530390
102	BEN	Sonio	SONIO	FR	886915427
103	BEN	MOSAE	SOTSIAALMINISTEERIUM	EE	998429731
104	BEN	SRC	VETENSKAPSRADET - SWEDISH RESEARCH COUNCIL	SE	999586165
105	BEN	TEDDY	TEDDY - EUROPEAN NETWORK OF EXCELLENCE FOR PAEDIATRIC CLINICAL RESEARCH	IT	910591963
106	BEN	TEKKARE	TEKKARE	FR	881967069
107	BEN	TIF	THALASSAEMIA INTERNATIONAL FEDERATION	CY	940669626
108	BEN	TUBITAK	TURKIYE BILIMSEL VE TEKNOLOJIK ARASTIRMA KURUMU	TR	999587135
109	BEN	RT (TuscReg)	REGIONE TOSCANA	IT	998823842
110	BEN	UAB	UNIVERSITAT AUTONOMA DE BARCELONA	ES	999986484
111	BEN	UCD	UNIVERSITY COLLEGE DUBLIN, NATIONAL UNIVERSITY OF IRELAND, DUBLIN	IE	999974359
112	BEN	UCSC	UNIVERSITA CATTOLICA DEL SACRO CUORE	IT	999915771
113	BEN	UEF	ITA-SUOMEN YLIOPISTO	FI	991207984
114	BEN	UKA	UNIVERSITAETSKLINIKUM AACHEN	DE	999897632
115	BEN	UKLFR	UNIVERSITAETSKLINIKUM FREIBURG	DE	999881918
116	BEN	UNICAMPANIA	UNIVERSITA DEGLI STUDI DELLA CAMPANIA LUIGI VANVITELLI	IT	999848356
117	BEN	UoC	PANEPISTIMIO KRITIS	EL	999588978
118	BEN	UGENT	UNIVERSITEIT GENT	BE	999986096

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Number	Role	Short name	Legal name	Country	PIC
119	BEN	UKCL	UNIVERZITETNI KLINICNI CENTER LJUBLJANA	SI	999882306
120	BEN	WDO	STICHTING WORLD DUCHENNE ORGANIZATION	NL	930321860
121	BEN	UU	UPPSALA UNIVERSITET	SE	999985029
122	BEN	c4c-S	CONECT4CHILDREN STICHTING	NL	881618063
123	BEN	CAU	UNIVERSITE CADI AYYAD	MA	998639930
124	BEN	CNRS	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS	FR	999997930
125	BEN	CIBER	CONSORCIO CENTRO DE INVESTIGACION BIOMEDICA EN RED M.P.	ES	997154957
126	BEN	UEFISCDI	UNITATEA EXECUTIVA PENTRU FINANTAREA INVATAMANTULUI SUPERIOR A CERCETARII DEZVOLTARII SI INOVARII	RO	972130024
127	BEN	UNIROMA1	UNIVERSITA DEGLI STUDI DI ROMA LA SAPIENZA	IT	999987745
128	BEN	UANTWERPEN	UNIVERSITEIT ANTWERPEN	BE	999902870
129	BEN	BNSF	BULGARIAN NATIONAL SCIENCE FUND	BG	984222335
130	BEN	Aalborg UH	REGION NORDJYLLAND (NORTH DENMARK REGION)	DK	997381064
131	BEN	RDB	REDKI BOLESTI BULGARIA	BG	880694720
132	BEN	BBMRI-ERIC	BIOBANKS AND BIOMOLECULAR RESOURCES RESEARCH INFRASTRUCTURE CONSORTIUM (BBMRI-ERIC)	AT	946597878
133	BEN	AarhusUH	AARHUS UNIVERSITETSHOSPITAL	DK	999643880
134	BEN	IABS-EU	ASSOCIATION INTERNATIONALE DE STANDARDISATION BIOLOGIQUE POUR L'EUROPE(IABS-EU)	FR	934774936
135	BEN	HRCI	HEALTH RESEARCH CHARITIES IRELAND COMPANY LIMITED BY GUARANTEE	IE	880683274
136	BEN	LMU	LUDWIG-MAXIMILIANS-UNIVERSITAET MUENCHEN	DE	999978433
136.1	AE	KUM	KLINIKUM DER UNIVERSITAT MUNCHEN	DE	995625946
137	BEN	MSW	MYSCIENCEWORK	FR	898132119
138	BEN	FNR	FONDS NATIONAL DE LA RECHERCHE	LU	998597153
139	BEN	NKFIH	NEMZETI KUTATASI FEJLESZTESI ES INNOVACIOS HIVATAL	HU	999578696
140	BEN	PEI	BUNDESINSTITUT FUR IMPFSTOFFE UND BIOMEDIZINISCHE ARZNEIMITTEL	DE	998217301
141	BEN	PLUS	PARIS-LODRON-UNIVERSITAT SALZBURG	AT	999868047

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Number	Role	Short name	Legal name	Country	PIC
142	BEN	SU	SORBONNE UNIVERSITE	FR	909875521
143	BEN	UNISI	UNIVERSITA DEGLI STUDI DI SIENA	IT	999898020
144	BEN	Vinnova	VERKET FOR INNOVATIONSSYSTEM	SE	999618757
145	BEN	CRG-CERCA	FUNDACIO CENTRE DE REGULACIO GENOMICA	ES	999544455
146	BEN	GMS-RS	REGION SKANE	SE	998165794
147	BEN	VIB	VIB VZW	BE	999651931
148	BEN	IPG	INSTITUT DE PATHOLOGIE ET DE GENETIQUE ASBL	BE	878266034
149	BEN	UO	UNIVERSITY OF OTAGO	NZ	998331567
150	BEN	HSJD	HOSPITAL SANT JOAN DE DEU	ES	997929890
151	AP	AZ	ASTRAZENECA AB	SE	999941379
152	AP	CHEO-RI	CHILDREN'S HOSPITAL OF EASTERN ONTARIO RESEARCH INSTITUTE INC	CA	907681187
153	AP	CIHR	CANADIAN INSTITUTES OF HEALTH RESEARCH	CA	960368386
154	AP	DFG	DEUTSCHE FORSCHUNGSGEMEINSCHAFT EV	DE	999547462
155	AP	FDB	FUJIFILM DIOSYNTH BIOTECHNOLOGIES UK LIMITED	UK	962770494
156	AP	FRQS	FONDS DE RECHERCHE DU QUEBEC - SANTE	CA	963122410
157	AP	HIPRA	HIPRA HUMAN HEALTH SL	ES	890821326
158	AP	LAB HIPRA	LABORATORIOS HIPRA SA	ES	991274041
159	AP	MICYRN	MICYRN	CA	880745451
160	AP	Miltenyi	MILTENYI BIOTEC BV & CO KG	DE	897602402
161	AP	Pfizer	PFIZER INC	US	887211374
162	AP	RCC	DEPARTMENT OF HEALTH GOVERNMENT OF WESTERN AUSTRALIA	AU	960480421
163	AP	REI	REITHERA SRL	IT	998129419
164	AP	RJF	LABORATORIO REIG JOFRE SA	ES	951005073
165	AP	ROCHE	F. HOFFMANN-LA ROCHE AG	CH	999601782
166	AP	SNSF	SCHWEIZERISCHER NATIONALFONDS ZUR FORDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG	CH	999540575
167	AP	UCB	UCB BIOPHARMA	BE	937666409
168	AP	Fraunhofer UK	FRAUNHOFER UK RESEARCH LIMITED	UK	952487039
169	AP	GA UK	GENETIC ALLIANCE UK LTD	UK	999790932
170	AP	UNEW	UNIVERSITY OF NEWCASTLE UPON TYNE	UK	999985417

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PARTICIPANTS

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Number	Role	Short name	Legal name	Country	PIC
171	AP	CUH	Cambridge University Hospitals NHS Foundation Trust	UK	991793961
172	AP	ULEIC	UNIVERSITY OF LEICESTER	UK	999985514
173	AP	QUB-UK	THE QUEEN'S UNIVERSITY OF BELFAST	UK	999992013
174	AP	UCL	UNIVERSITY COLLEGE LONDON	UK	999975620
175	AP	UCAM	THE CHANCELLOR MASTERS AND SCHOLARS OF THE UNIVERSITY OF CAMBRIDGE	UK	999977172

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LIST OF WORK PACKAGES

Work packages

Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
WP1	Coordination and management	1 - INSERM	607.00	1	84	D1.1 – Data Management Plan D1.2 – Annual Work Plan Y2 D1.3 – Annual Work Plan Y3 D1.4 – Annual Work Plan Y4 D1.5 – Annual Work Plan Y5 D1.6 – Annual Work Plan Y6 D1.7 – Annual Work Plan Y7 D1.8 – Periodic Progress Report 1 D1.9 – Periodic Progress Report 2 D1.10 – Periodic Progress Report 3 D1.11 – Periodic Progress Report 4 D1.12 – Periodic Progress Report 5 D1.13 – RDP SRIA Update D1.14 – Report on cumulative expenditure incurred
WP2	Communication and dissemination	2 - TEAMIT	72.00	1	84	D2.1 – Project website D2.2 – Communication and dissemination strategy
WP3	Joint Transnational Calls for collaborative research projects	3 - DLR	132.00	1	84	D3.1 – Joint Transnational Call documents 1 D3.2 – Joint Transnational Call documents 2 D3.3 – Joint Transnational Call documents 3 D3.4 – Joint Transnational Call documents 4

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Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
						D3.5 – Joint Transnational Call documents 5 D3.6 – Joint Transnational Call documents 6 D3.7 – Joint Transnational Call documents 7 D3.8 – Evaluation Report of the JTCs 1 D3.9 – Evaluation Report of the JTCs 2 D3.10 – Evaluation Report of the JTCs 3 D3.11 – Evaluation Report of the JTCs 4 D3.12 – Evaluation Report of the JTCs 5 D3.13 – Evaluation Report of the JTCs 6 D3.14 – Evaluation Report of the JTCs 7
WP4	Clinical trial call management	5 - FTELE	28.00	1	84	D4.1 – Clinical Trial Call documents D4.2 – Evaluation Report of the Clinical Trial Call
WP5	Networking to share knowledge	6 - LMT	22.00	1	84	D5.1 – NSS Call documents D5.2 – List of funded networks 1 D5.3 – List of funded networks 2
WP6	Diagnostic data availability	8 - UT	614.00	1	84	D6.1 – Roadmap for genomic federated data analysis approach D6.2 – Research dataset on returned diagnostic results 1 D6.3 – Research dataset on returned diagnostic results 2
WP7	Genome re-analysis research pipeline	10 - CNAG	490.00	1	84	D7.1 – Coordinated re-analysis diagnostic pipeline D7.2 – Best practice guidelines for

Work packages

Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
						diagnostic re-analysis & reinterpretation strategies
WP8	Innovation to shorten time to RD diagnosis	11 - SRUMC	347.00	1	84	D8.1 – Software for long-read pipelines optimized for RD diagnoses D8.2 – Software update for integrated DNARNA pipeline optimized for RD discoveries 1 D8.3 – Software update for integrated DNARNA pipeline optimized for RD discoveries 2 D8.4 – Software for multi-omics pipeline optimized for RD discoveries 1 D8.5 – Software for multi-omics pipeline optimized for RD discoveries 2
WP9	Real World Data	13 - UKHD	633.00	1	84	D9.1 – Regulatory grade cohort Inventory D9.2 – Individual disease progression models D9.3 – Drug Development Tools
WP10	Clinical Outcome Assessment	15 - VHIR	336.00	1	84	D10.1 – Disease burden and cost of illness framework for RDs D10.2 – Platform for development of regulatorygrade patient-relevant COAs in RD D10.3 – Toolbox on collection of patient selfreported data
WP11	ATMPs	1 - INSERM	210.00	1	84	D11.1 – Result of the PoC studies for ATMP technologies D11.2 – ATMP technology Platform validated in clinical context

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Work packages

Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
WP12	N-of-few Approach	16 - LUMC	82.00	1	84	D12.1 – Assessment criteria for patient eligibility to individualised ASO treatment D12.2 – Toolkit on outcome measures for N-of- 1 D12.3 – Standardized platform for timely development of ASO individualized treatments
WP13	RD Virtual Platform (RD-VP) finding and accessing the data ecosystem	1 - INSERM	230.00	1	84	D13.1 – VP specifications and documentation 1 D13.2 – VP specifications and documentation 2 D13.3 – VP specifications and documentation 3
WP14	Data readiness services	16 - LUMC	168.00	1	84	D14.1 – Data Stewardship Wizard with the compilation of data models and data preparation workflows 1 D14.2 – Data Stewardship Wizard with the compilation of data models and data preparation workflows 2 D14.3 – Data Stewardship Wizard with the compilation of data models and data preparation workflows 3
WP15	Data sharing and analysis services	19 - UMCG	224.00	1	84	D15.1 – Portfolio of ERDERA large scale analysis services and pipelines D15.2 – Portfolio of ERDERA federated analysis methods and services D15.3 – Technical guidelines for the implementation of services used in the use cases on federated analysis

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Work packages

Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
WP16	Knowledge bases and ontologies for RD research	20 - AUMC	250.00	1	84	D16.1 – First standard application of multidimensional knowledge networks (RD maps) addressing an RD case D16.2 – First version of ontologies (antenatal phenotypes and functional impacts) integrated with ORDO D16.3 – Treatabolome demonstrator D16.4 – Knowledge bases and ontologies for PROM/PCOM, disabilities and Treatabolome
WP17	Mentoring and consultancy	22 - EATRIS	38.00	1	84	D17.1 – Recommendations to funders on addressing translatability of projects through funding opportunities D17.2 – Result of feasibility study for consultancy-based expertise services D17.3 – Final report of the mentoring services activity
WP18	Regulatory support service	23 - FGB	88.00	1	84	D18.1 – Set of regulatory recommendations for CRNs D18.2 – Set of Regulatory support tools for preclinical development to facilitate regulatory filings and convergence for RD D18.3 – Roadmap for physical and written standards for quality control of ATMPs D18.4 – Summary report of ERDERA Qualification applications with regulatory Authorities
WP19	Methodological support	24 - APHP	158.00	1	84	D19.1 – First knowledge transfer of

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Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
						protocols & tools to CRN and selected JTC projects D19.2 – Final knowledge transfer of protocols & tools to CRN and selected JTC projects D19.3 – First protocol & tools for methodological upscaling of RD research projects D19.4 – Final protocol & tools for methodological upscaling of RD research projects
WP20	Education and Training on RD Research	26 - EURORDIS	318.00	1	84	D20.1 – Report on the identification and fulfilment of RD education and training needs D20.2 – Impact assessment of ERDERA education and training programme
WP21	Technology accelerator	28 - UC	563.00	1	60	D21.1 – Base protocols for research grade rAAVs production D21.2 – Computational tools for of LNPs, EVs and biohybrids formulation development D21.3 – gRNAs for effective and safe gene editing D21.4 – Dataset of Gene therapy Immunogenicity assessment on humanized mouse model D21.5 – Multiomics single cell analysis and bioinformatic pipeline fit-for-purpose qualified to characterize immune response to ATMPs

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Work packages

Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
						D21.6 – Report on standard regulatory quality control parameters of mRNA formulations D21.7 – Regulatory compliant recommendations for rAAV analytics
WP22	Public-Private Collaboration accelerator	29 - FFRD	125.00	1	84	D22.1 – Accelerator Hub inclusion criteria for research projects D22.2 – Impact analysis of Accelerator hub outputs 1 D22.3 – Impact analysis of Accelerator hub outputs 2
WP23	NMGs promotion and national alignment	1 - INSERM	330.00	1	84	D23.1 – Best practice guidelines for creation and promotion of NMGs D23.2 – First report on the impact of NMGs D23.3 – Second report on the impact of NMGs D23.4 – Recommendations on the NMG sustainability
WP24	Fostering engagement of underrepresented countries in ERDERA	32 - AICIB	135.00	1	84	D24.1 – Mapping of UCs specific needs and expectations 1 D24.2 – Mapping of UCs specific needs and expectations 2 D24.3 – Focused guidelines for actions at the National level 1 D24.4 – Focused guidelines for actions at the National level 2 D24.5 – Guidelines to increase UCs integration in ERDERA (including in funding activities) 1

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Work packages

Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
						D24.6 – Guidelines to increase UCs integration in ERDERA (including in funding activities) 2 D24.7 – Guidelines to increase UCs integration in ERDERA (including in funding activities) 3
WP25	ERDERA Global Collaborations	7 - ZonMw	155.00	1	84	D25.1 – White paper on ERNs Living Lab 1 D25.2 – White paper on ERNs Living Lab 2 D25.3 – Sustainability Plan for established strategic alliances and partnerships D25.4 – Publication on the International CRNs
WP26	Ethics requirements	1 - INSERM	0.00	1	84	D26.1 – OEI - Requirement No. 1 D26.2 – OEI - Requirement No. 2 D26.3 – OEI - Requirement No. 3 D26.4 – OEI - Requirement No. 4 D26.5 – OEI - Requirement No. 5 D26.6 – OEI - Requirement No. 6 D26.7 – OEI - Requirement No. 7 D26.8 – OEI - Requirement No. 8

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Work package WP1 – Coordination and management

Work Package Number	WP1	Lead Beneficiary	1 - INSERM
Work Package Name	Coordination and management		
Start Month	1	End Month	84

Objectives
To provide the necessary support for efficient management and coordination of the ERDERA.

Description
T1.1. Day-to-Day management and coordination (M1-M84) TL: INSERM_IT-GGB; Contributors: TEAMIT. Day-to-day management and coordination of the project will be ensured by the coordination team based at INSERM, providing support, and overseeing various aspects, including communication, risk management, and reporting, drawing from the experience of the well-structured EJP RD management office. T1.1. will focus on the planning and reporting related to the contractual obligations included in the Grant Agreement, with the development of the Annual Work Plans and Annual Progress report, including setting up reporting mechanisms, supporting, and training Beneficiaries on reporting procedures and coordinating the production of reports. Risk management is also a priority, identifying, assessing, and following up on threats and opportunities likely to affect the project performance. Additionally, ERDERA will develop a sustainable Data Management Plan ensuring data accountability, reliability, and compliance with IP, ethical, FAIR, and GDPR regulations. It will cover aspects such as data handling, types of data, methodology, sharing and access, curation, preservation, ethical and legal compliance. T1.1. aligns with GO1-3; SO5; OO3,5. T1.2. Governance & strategy (M1-M84) TL: INSERM_IT-GGB; Contributors: TEAMIT, EURORDIS, GA UK*, HRCI, AFM, WDO, RDI. T1.2. aims to establish a governance and a strategy framework for the partnership. The Coordination team (INSERM) will assist all governance and advisory bodies by providing the necessary tools (e.g., secured space for exchange and document storage, voting system), documents (required analyses, working documents, relevant drafts) and prepare the agendas. Additionally, public consultations will be organized, and the Strategic Research and Innovation Agenda (SRIA) will be updated through stakeholder engagement, environmental scanning, including progress and possible synergies with the EU Cancer Mission and the EU Beating Cancer Plan, and SWOT analysis. Patient and Public Involvement & Engagement (PPIE) will be embedded throughout ERDERA, with a core PPIE group guiding engagement practices and ensuring patients' needs are prioritized. T1.2. aligns with GO1-3; SO5; OO3,5. T1.3. Monitoring of the Partnership activities (M1-M84) TL: TEKKARE, CVBF; Contributors: INSERM_ITGGB, ELS,,MSW, CSO-MOH, ANR, FFRD, DLR, ISCIII, ZonMw, LMT, TEAMIT. Monitoring of ERDERA's activities and effectiveness is a key element of T1.3., guaranteed by a multi-level approach, including tracking specific Key Performance Indicators (KPIs), assessing performance at various levels, and collecting data to support decision-making and sustainability planning. This task will also consider criteria on ERDERA Results exploitability by non-rare conditions; application of these criteria to funded research activities will be considered in the funding opportunities, as well as criteria for under-represented countries involvement (widening). ST1.3.1. aims to leverage existing infrastructure and APIs to create a cost-effective, efficient software solution for data collection and monitoring that will constitute a comprehensive monitoring system for the Partnership's needs. ST1.3.2. is about the monitoring of the Partnership's activities across multiple levels: Level 1 - ERDERA as a whole; Level 2 - WPs performance; Level 3 - monitoring of funded projects; Level 4 - governance and strategy. T1.3. aligns with GO1-3; SO5; OO3,5. T1.4. Sustainability strategy (M1-M84) TL: CE; Contributors: INSERM_IT-GGB, TEAMIT. T1.4. is focused on ensuring both the short-term and the long-term vision and viability of the ERDERA through a continuous monitoring and support for IPR and results requiring legal assistance to ensure long-term sustainability; and the development of a plan and procedures for transitioning from a partnership to establishing a self-sustaining institute with its own legal status. It involves managing IP, identifying exploitable results, and preserving consortium interests through a Consortium Agreement. Additionally, it encompasses long-term sustainability planning, emphasizing the value of collective services and data-driven decision-making. The strategy includes defining the vision, mapping business models, and proposing a suitable legal framework while considering costs, financing, and income generation potential, ensuring the Institute's sustained growth within the RD ecosystem. In building the sustainability strategy, the first grant instalment for three years and the output of this period will allow for an in-depth exploration of other sustainability strategies, beyond the institute (for ERDERA as a whole), including sustainability options of the different outputs, fostering ownership of the results by the contributing organisations and the Member States. ERDERA accelerator Hub will also facilitate contacts with potential investors. T1.4. aligns with GO1-3; SO5; OO3,5. T1.5. Ethics compliance (M1-M84) TL: FGB; Contributors: INSERM_IT-GGB. To guarantee and support ethics

compliance of all project activities, an internal Ethics Advisory Group (EAG) will be set up and composed of ethics experts delegated by beneficiaries. Support will be provided on ethics issues/concerns raised during the implementation of the project and its research activities. This activity will also include the ethics assessment and/or follow-up of funded projects. Different ethics aspects will be addressed according to the Horizon Europe ethics guidance including but not limited to animal welfare, research with humans, data processing activities, involvement of children, AI methods, etc. An Independent Ethics Advisor (IEA) will be appointed to monitor adherence to European ethical and legal frameworks, offering guidance on various aspects, including Data Management Plan. This comprehensive task ensures that ethical standards and compliance are upheld throughout the partnership's lifecycle. T1.5. aligns with GO1-3; SO5; OO3,5.

Work package WP2 – Communication and dissemination

Work Package Number	WP2	**Lead Beneficiary**	2 - TEAMIT
Work Package Name	Communication and dissemination		
Start Month	1	**End Month**	84

Objectives

To pave the way for future sustainability of results and outcomes by ensuring broad visibility and understanding that lead to acceptance and uptake, thus, maximising the impact of ERDERA.
Specific objectives:
(1) Raise awareness about ERDERA vision and mission and continue the process initiated by EJPRD of positioning this ambitious programme as a pivotal actor to advance RD research and build the RD ecosystem in Europe and beyond;
(2) Communicate progress, promote resources and services, and disseminate results to build ERDERA's reputation as an enabler of innovative, standardised, streamlined, and collaborative transnational RD research;
(3) In collaboration with all work streams and partners' comms representatives, maximise outreach and contribute to foster engagement, knowledge exchange, community building, use of services and uptake of results; and
(4) Support all WPs in their communication needs, facilitating consistency and alignment with the overall communication strategy, plans, and materials.

Description

T2.1. Communication and dissemination strategy (M1-M84). TL: TEAMIT, INSERM_IT-GGB. T2.1. will design a communication (C) and dissemination (D) strategy for ERDERA by M6, tailored to specific audience groups' needs and preferences. This strategy will observe Open Science principles and support and enhance ERDERA overall objectives. A comprehensive audience analysis, initially informed by representatives of all work streams and partners' communication experts, which will constitute the backbone of the C&D strategy. This will be led by the senior communications manager and will include: (1) SWOT analysis that incorporates learnings, achievements, and resources from EJPRD; (2) clear C&D objectives and a set of key messages (generic and specific for each audience group); (3) mapping of audiences, matched with appropriate communication channels and tools (comms. matrix); (4) KPIs to feed into T1.3 for regular evaluation of C&D strategy performance; and (5) explicit roles and responsibilities. T2.1. aligns with GO:3; SO:3,5; OO:3,5.
T2.2. C&D operational plans (M6-M84). TL: TEAMIT, INSERM_IT-GGB. The C&D strategy will be implemented through annual work plans designed by T6.2 with the concurrence of WPLs and based on the analysis of the performance evaluation conducted in WP1. These will include SMART objectives, operational pillars, or a pre-emptive calendar of activities, which are audience specific. An editorial plan, led by a scientific writer, will be developed that constructs and supports a coherent ERDERA narrative to drive forward cutting edge ERDERA research, using case studies, personal testimonies, etc. T2.2. will be responsible for the implementation, coordination with partnering organisations and monitoring of annual plans and will collect quarterly KPIs for subsequent evaluation. Finally, specific tactical plans for singled-out tasks will be developed (i.e., coordinated promotion of joint calls) as described in T2.3. A communications officer, with expertise on digital channels, will support the successful delivery of planned activities. T2.2. aligns with GO:3; SO:3; OO:3,5.
T2.3. Synergies with work streams and communication tools (M1-M84) TL: TEAMIT. Contributors: INSERM_IT-GGB, EURORDIS, WDO, FFRD, TEDDY. T2.3. will leverage channels, tools, and resources generated by EJP RD to develop ERDERA branding, including communication platforms and materials (website, newsletter, videos, infographics, factsheets, social media assets, etc) to support ERDERA in all communication and dissemination needs. This transversal WP will synergise with all work streams, and will specifically play an active role in: (1) coordinated

promotion of all funding calls (joint translational, Clinical Trials (CTs) and knowledge sharing), including featuring the progress being made in each funded project and disseminating key results; (2) increase awareness of ERDERA assets and services (data services hub/virtual platform, acceleration hub, knowledge hub, CRNs, training, mentoring); (3) contribute to promote related activities, present case studies and disseminate results; and (4) support outreach and inter(national) capacity alignment activities that includes IRDiRC
communications strategy. T2.3. aligns with GO:3; SO:2,3,5; OO:3-5.

Work package WP3 – Joint Transnational Calls for collaborative research projects

Work Package Number	WP3	**Lead Beneficiary**	3 - DLR
Work Package Name	Joint Transnational Calls for collaborative research projects		
Start Month	1	**End Month**	84

Objectives
Implementation of seven joint transnational EC co-funded calls through the following tasks: (1) Topics selection and definition of eligibility criteria; (2) JTCs call implementation; and (3) Patient engagement.

Description
T3.1. Call topic selection for JTCs and Clinical Trial (CT) Calls (M1-M84) TL: ANR, DLR, ISCIII, FFRD, FTELE; Contributors: ZonMw, WDO, EURORDIS, all participating funding agencies (BMBF, BNSF, CIHR, CSO-MOH, DFG*, ETAg, F.R.S.-FNRS, FCT, FNR, FRQS, FRRB, FWF, FWO, HRB, IFD, IT-MOH, LMT, LZP, MOSAE, MUR, MZd, NCBR, NKFIH, Rannis, RCN, RIF, RT (TuscReg), SAS, SNSF, SPW, SRC, TUBITAK, UEFISCDI, Vinnova). Identification of topics for the JTCs and CTs calls will be centralised under T3.1. and will include multi-stakeholder input from the RD community inside and outside ERDERA, as well as IRDiRC, and lessons learned from previous E-Rare and EJP RD calls. It is envisioned to formulate a multi-annual call topic strategy with broader themes in consultation with the ERDERA MAB. To maximize synergies, it is expected that the topics for the first three calls will be in line with the CRN themes diagnosis, therapy development, and improved understanding of clinical outcomes. Themes in years 4-7 will take advantage of ATMP technology advancement knowledge derived from WP11 and WP21 as well as facilitate early career researchers and human and social sciences research among other possible themes which will be closely linked to the developments in the CRNs and accelerator hub. To avoid conflicts of interest, a strict firewall between the parties deciding on call topics and partnership beneficiaries will be established. T3.1. aligns with GO:1-3; SO:1-5; OO:1-5. T3.2. JTC implementation (M1-M84) TL: DLR, ANR, FFRD, ISCIII; Contributors: all participating funding agencies (BMBF, BNSF, CIHR, CSO-MOH, DFG*, ETAg, F.R.S.-FNRS, FCT, FNR, FRQS, FRRB, FTELE, FWF, FWO, HRB, IFD, IT-MOH, LMT, LZP, MOSAE, MUR, MZd, NCBR, NKFIH, Rannis, RCN, RIF, RT (TuscReg), SAS, SNSF, SPW, SRC, TUBITAK, UEFISCDI, Vinnova, ZonMW). T3.2. aligns with GO:1-3; SO:1-5; OO:1-5. ST3.2.1. Preparation of the joint transnational calls and establishment of the joint call secretariat: The TL will be responsible for facilitating the definition of eligibility criteria as well as drafting and finalizing all necessary documents including Memorandum of Understanding, Call text, Governance, and evaluation procedures, Guidelines for applicants, Proposal templates. In addition, ST3.2.1. will set up the JCS which will act as central support to the applicants regarding all aspects of proposal drafting and submission. The call for proposals will be published on all relevant channels. The call will be opened for the submission of proposals for at least 60 days. Shortly after publication, a webinar will be held to inform applicants of the call specifics. ST3.2.2. Scientific evaluation of the joint transnational calls: The evaluation will be implemented in a two-step procedure according to the Horizon Europe rules. In the first step, applicants are invited to submit pre-proposals. The eligible applications will first undergo national eligibility check and then be submitted to the transnational peer review Scientific Evaluation Committee (SEC) composed of independent expert scientists chosen for their scientific, technical, patient and disease-specific expertise. The evaluation of proposals will be aligned on the scoring system and criteria of Horizon Europe. The SEC will select the most promising applications for submission of a full proposal. The full proposal step will be used to facilitate inclusion of additional partners from underrepresented countries through a voluntary widening step. Applicants will be able to receive advice on ethical, regulatory, innovation, translational, and data management aspects from ERDERA services and can modify their proposals accordingly. The submitted full proposals will be reviewed by three members of the previously established SEC. These will be complemented by patient experts and methodological experts. The SEC will agree on a final ranking list of excellent proposals recommended for funding. In addition, an

independent expert will be invited as official observer to the second SEC meeting. The assessment of the observer will be provided in a report to the European Commission.
ST3.2.3. Ethics evaluation of projects recommended for funding: An ethics evaluation of the projects selected for funding will be done by independent ethics evaluators following Horizon Europe standards. Only projects that pass the ethics evaluation will be funded. ST3.2.4. Funding decision and kick-off: The Call Steering Committee of participating funders (CSC) will take its final funding decision based strictly on the scientific recommendation of the SEC (ranking list). Each eligible applicant will be funded by the organization of the country/region from which the applicants have applied and according to the national/regional administrative regulations (virtual common pot model). The applicants will be informed about the final funding decision and the national negotiations will commence. An online kick-off meeting will be held for the selected projects.
ST3.2.5. Quality management of call procedures: The practicability of administrative and operational mechanisms used for implementation of calls, peer review, funding of projects, and scientific follow-up will be monitored by the JCS with feedback from all participating stakeholders. The lessons learned will feed the call design and implementation of the next joint calls.
T3.3. Engagement of patients in research project funding (M1-M84) TL: EURORDIS, FFRD, DLR; Contributors: ANR, ISCIII, ZonMw, RT (TuscReg), WDO, AFM. The working group will focus on improving patient involvement and engagement on all levels of the call process (e.g. call topic definition/eligibility issues for PAOs participation and/or funding/dissemination/evaluation/PPIE-oriented monitoring indicators), but also engagement in research project design. It will facilitate call dissemination and promotion to PAOs. T3.3. aligns with GO:1-3; SO:1,3-5; OO:1,4,5.

Work package WP4 – Clinical trial call management

Work Package Number	WP4	**Lead Beneficiary**	5 - FTELE
Work Package Name	Clinical trial call management		
Start Month	1	**End Month**	84

Objectives
(1) Develop the call framework; (2) Open the call and select CTs for funding; (3) Secure proper project implementation, milestones monitoring and financial management; and (4) Leverage the work of the CRN both for the design and the implementation of the studies that will therefore become “demonstrators” of the potential of the CRN itself.

Description
T4.1. Develop the call framework (M1-M18) TL: FTELE, DLR, WDO, QUB-UK*; Contributors: HRB. The partners will define and finalize the text of the call by M18, including timing for proposal submission. The call topic selection and design will be in line with the processes described and in close collaboration with WP3, T3.1. Specifically, this will be an open competitive call, open to researchers, clinical centres, and patient organizations from all Horizon Europe eligible countries. The call text will clarify the eligibility criteria. A minimum of recruiting centres and/or countries will be specified, and the number and role of each centre and partner will need to be defined in the application. The potential roles for companies will be specified and guidelines about their nvolvement (at each stage of the call and of the project) will be provided. The design of the call will consider the model under development by ERA4Health to demonstrate the feasibility of the funding model. The MAB or specific Thematic Groups that could stem from it will be involved in the discussion. The goal is to develop a funding model that overcome bottlenecks encountered under JTC2016 E-Rare-3 and fund multinational RD CTs. In addition, ERDERA will contribute to the Accelerating Clinical Trials in the EU (ACT EU) initiative via ECRIN to integrate their recommendations for multinational CTs in the call text of the ERDERA CTs’ calls. The final call documents will be presented to the Board of Funders for their approval. T4.1. aligns with GO:2; SO:3; OO:1,5. T4.2. Open the call and select trials for funding (M19-M43) TL: FTELE; Contributor: WDO. FTELE will open the first call by M19. The second call will be open by M31. The evaluation process for the applications will include POs patient experts or CABs when available, clinical experts, and experts in trial design and methodology who will provide reports to the group responsible for making the decision. Applicants will be given an opportunity to respond to the peer review after the full proposal evaluation. This will ensure the selection of clinical trial proposals which would adhere to the call requirements, fulfil the eligibility criteria, highest scientific merit, and has potentially a meaningful impact for patients. As a National Research Funding Organisations (RFOs), Fondazione Telethon will establish a call secretariat, and it will manage all the activities related to this task, as well as liaise with other partners if required. Special attention will be

given to patient-centricity and patient involvement in the proposal and during the project's implementation. Conflict of interest (COI) will be managed for all evaluators. T4.2. aligns with GO:2; SO:3,4; OO:1,4,5.
T4.3. Project implementation, project monitoring, and financial management (M38-M84) TL: FTELE; Contributors: IT-MOH, CSO-MOH, WDO. T4.3. will ensure a smooth implementation of the funded trials and follow the achievement of project specific milestones for each funded clinical trial, while it will promote meaningful and impactful research. For each project, funding will be paid in instalments, which will be triggered by the achievement of specific milestones. This is therefore a crucial task to ensure an efficient use of resources. T4.3. aligns with GO:2; SO:1; OO:1,5. This WP comprises two Subtasks: ST 4.3.1. Project implementation and reporting on milestone achievements. ST 4.3.2. Financial management with UPPMD as contributor.

Work package WP5 – Networking to share knowledge

Work Package Number	WP5	**Lead Beneficiary**	6 - LMT
Work Package Name	Networking to share knowledge		
Start Month	1	**End Month**	84

Objectives

To share knowledge on research among relevant transnational European and transcontinental RD stakeholders including clinicians, basic researchers, patients' organisations/RD support groups, as well as PhD students, post-docs and early career researchers, and industry. To implement the networking support scheme for building new European and global research networks or expanding existing research networks on RDs and rare cancers to support patient-centred research, and to include stakeholders of widening countries and young
researchers. Realisation of this scheme will address OO5 and will contribute to OO1, OO4, SO3, SO4, SO5, GO1, GO2 and GO3, ensuring knowledge flow and bringing together teams for patient-oriented R&I. Therefore, WP5 will synergize with R&I funding work stream of ERDERA (WP3 and WP4) and could facilitate collaborations (including cross-sectoral) at national, European, and global levels (WP23, WP24 and WP25).

Description

T5.1. Preparation and launching of the funding scheme (M1-M9) TL: LMT, ZonMw; Contributors: FFRD, ANR, EURORDIS, WDO, GA UK*, CSO-MOH, FGB. A call secretariat will be set up and a working group will be formed to prepare call documents (e.g. call text, application template, documents for evaluation procedures and documents for funding of selected networks). The task includes the call launch, building a pool of scientific evaluators (clinicians, researchers, PAO representatives/patients), and preparation of webinar(s) for
potential applicants. When the scheme is launched, the funding opportunity will be continuously open with 2 collection dates per year. T5.1. aligns with GO:1-3; SO:3-5; OO:1,4,5.
T5.2. Evaluation of the selected proposals after each collection date (M9-M84) TL: LMT, ZonMw; Contributor: FGB. T5.2. will be executed by the call secretariat and comprises of subsequently the following activities: (1) Eligibility check of received applications; (2) Scientific evaluation by the pool of evaluators including patient experts, using the EC Horizon Europe scientific evaluation criteria; (3) Ethics assessment process: This will be performed in the framework of Task 1.6 for the applications that are positively evaluated for
funding by the scientific evaluators. The process will consist of evaluating the ethics dimension of the projects and releasing specific ethics requirements to be fulfilled and ethics recommendations to be implemented for each proposal. Attention will be paid to the GDPR compliance for Third Countries (non-EU Member States or EEA countries) on sensitive personal health data. The ethics assessment process will be performed for each round of the call; and (4) Funding decision by the s based on the results of the scientific evaluation and the ethics assessments. T5.2. aligns with GO:1-3; SO:3-5; OO:1,4,5.
T5.3 Quality management (M9-M84) TL: LMT, ZonMw; Contributors: FFRD, ANR, EURORDIS, WDO, GA UK*, CSO-MOH, FGB. T5.3 aims to spotlight the practicability of administrative and operational mechanisms used for implementation of the scheme trying to balance the benefit-to-work ratio and with support of WP coordination/ monitoring perform the networks follow-up and monitoring. T5.3 will be performed by the call secretariat with support and feedback from the working group (T5.1. leaders, contributors including the partners responsible for overall ERDERA ethics compliance and scientific monitoring (WP1). The quality of the implementation of the funding scheme will be periodically assessed. Results of this quality management process will be incorporated in the lessons learned reports. The outcomes from each evaluation round will feed the implementation of next collection dates to facilitate the evolution

of robust and functional administrative and operational practices and ensure a continuous process improvement. T5.3. aligns with GO:1-3; SO:3-5; OO:1,4,5.

Work package WP6 – Diagnostic data availability

Work Package Number	WP6	Lead Beneficiary	8 - UT
Work Package Name	Diagnostic data availability		
Start Month	1	End Month	84

Objectives

(1) Coordinate and consolidate the diagnostic data availability and collation effort in the CRN diagnostic workstream that is based on the existing ERN-led ecosystem, and also comprises national UDPs, national diagnostic centres, programs and national mirror groups; (2) Implement data standardisation, sharing, federation and quality control so that data research re-analysis methodologies can be applied for solving unsolved RD patients and to shorten time to diagnosis; and (3) Ensure access to the data during the project to enable re-analysis of large datasets. This allows a quick return of research results to the clinics, and to RD patients and their families.

Description

T6.1. Coordinate and consolidate the diagnostic research data availability and collation effort in the diagnostic research workstream (M1-M84) TL: UT, CNAG, UTARTU. Contributors: CRG-CERCA, UMCG, CIBER, ISCIII, Aalborg UH, Aarhus UH, AOU Meyer IRCCS, APHP, CCRI GmbH, CHU Dijon, Erasmus MC, IBG, IGC PAN, INSERM_IT-GGB, INSERM_U1112, INSERM_U974, MUS, RCSI, REGIONSYD, UCAM, UNEW, UKCL, UNICAMPANIA, UNISI, UoC, VIB, VULSK, UO, ERN HCPs, diagnostic centres and RD NMGs throughout Europe linked to ERNs and UDPs.
T6.1. will focus on coordinating and consolidating the CRN diagnostic research workstream. The following activities will be pursued: (1) Establish and operate a Data Availability Committee to coordinate data availability activities (distributed/federated approaches); (2) Consolidate research and data policies and agreements in line with 1+MG and GDI; (3) Consolidate standards, minimum quality criteria and processes for omics, phenotypic and meta-data availability and collation in line with GDI and 1+MG; (4) Set up a working group that comprises the different stakeholders (1+MG RD use case, GDI, ERNs and diagnostic centres, ERDERA data service hub) to prepare, pilot, and scale-up the federated data collation approach; (5) Qualify participating ERNs, UDPs, and diagnostic centres in line with 1+MG/GDI, cooperating closely with capacity building in WP20; (6) Establish a network of diagnostic research centres in underrepresented countries based on NMGs, ERNs, Joint Action JARDIN, and 1+MG; and (7) Implement the CRN diagnostic research data management system developed in WP15. T6.1. aligns with GO:1; SO:2,5; OO:3,5.
T6.2. Data standardisation, sharing, and federation (M1-M84) TL: CNAG, UTARTU, CAD. Contributors: UT, CRG-CERCA, UMCG, RS, GMS-RS, NKUA, UANTWERPEN, IPG,UO, Aalborg UH, Aarhus UH, AOU Meyer IRCCS, APHP, CCRI GmbH, CHU Dijon, Erasmus MC, IBG, IGC PAN, INSERM_IT-GGB, INSERM_U1112, INSERM_U974, MUS, RCSI, REGIONSYD, UCAM, UNEW, UKCL, UNICAMPANIA, UNISI, UoC, VIB, VULSK, UO ERN HCPs, diagnostic centres throughout Europe linked to ERNs, RD NMGs and UDPs.
T6.2. will serve the CRN Diagnostic Research ecosystem by collating REAL (RE-Analysis Logistics) datasets from undiagnosed patients enabling both distributed and federated re-analysis approach. The following activities will be pursued: (1) Establishment of a CRN diagnostic research data availability helpdesk; (2) Making available and federate standardised pheno-clinical information, genomic data (including exomes (Y1-3), short-read (Y1-Y7) and long-read genomes (Y4-Y7) and other omics datasets to serve WP7 and WP8 following standards and quality criteria consolidated in task 6.1.; (3) Ensure all clinical information and metadata is linked to the CRN data management system and files are made available to task 6.3 for distribution across data hubs of the CRN diagnostic research workstream and for returning of research results; (4) Implementation of an automated data quality control system to ensure minimum data quality standards establish in 6.1 are met for delivering reliable results in WP7 and WP8. T6.2. aligns with GO:1; SO:2,5; OO:2.
T6.3. Data access and returning research results (M1-M84) TL: UT. Contributors: CNAG, CRG-CERCA, UMCG, CAD, RS, GMS-RS, NKUA, UANTWERPEN, CENTOGENE, IPG, UO, Aalborg UH, Aarhus UH, AOU Meyer IRCCS, APHP, CCRI GmbH, CHU Dijon, Erasmus MC, IBG, IGC PAN, INSERM_IT-GGB, INSERM_U1112, INSERM_U974, MUS, RCSI, REGIONSYD, UCAM, UNEW, UKCL, UNICAMPANIA, UNISI, UoC, VIB, VULSK, UO, ERN HCPs, diagnostic centres throughout Europe linked to ERNs and UDPs, RD NMGs.
T6.3. will establish a secure and collaborative data framework that encompasses data access, transfer and distribution as well as returning diagnostic research results for federated and distributed approaches. The following activities will be

pursued: (1) Alignment with WP14 and WP15 task 15.1 to integrate metadata information and data transfer procedures in the CRN Diagnostic Research management system; (2) Planning data access for research re-analysis, including analysis results (Y1-3); (3) Data transfer from the CRN diagnostic workstream entry points (task 6.2) to points of data analysis according to the needs of WP7 and WP8; (4) Utilising the CRN diagnostic research data management system to return research results following GA4GH policy recommendations in a timely manner including monitoring time-todiagnosis; (5) Periodic submission of relevant variant results information to international public databases like ClinVar. With WP14, we will promote a federated data sustainability model relying on GDI national nodes (e.g. Federated EGA), although central EGA in Barcelona will provide central sustainability until federated model is available (and for partners that cannot submit to a national node). T6.3. aligns with GO:1; SO:2,5; OO:2.

Work package WP7 – Genome re-analysis research pipeline

Work Package Number	WP7	**Lead Beneficiary**	10 - CNAG
Work Package Name	Genome re-analysis research pipeline		
Start Month	1	**End Month**	84

Objectives

(1) Coordinate a pan-European genomics diagnostic research pipeline beyond the state-of-the-art diagnostic pipeline; (2) Re-analyse existing data moving from a distributed to a federated one to discover new molecular diagnoses from known, and novel, disease-gene associations; (3) Leverage knowledge and develop best practices to improve variant interpretation across disease groups and ERNs and discover new gene-disease associations; and (4) Facilitate the adoption of knowledge, prepare and share best practice guidelines across disease groups and ERNs.

Description

T7.1. Exome and genome re-analysis pipeline coordination and monitoring (M1-M84) TL: UT, CNAG, SRUMC; Contributors: CHU DIJON, UNEW*, UGENT, ISCIII-IIER, CAD, UU, CENTOGENE, CHEO-RI*, UMCG, EURORDIS, CIBER.

T7.1. will establish one Data Analysis Task Force (DATF) and three super-Data Interpretation Task Forces (DITFs) to bring together the expertise from data analysis and clinical researchers. The committee will jointly coordinate and monitor the continuously revised CRN standard diagnostic research pipeline for REAL data sets (e.g. phenotype, pedigree and genetic data), which should be applicable in both a distributed and federated manner (based on Solve-RD, using GRCh38). The committee will also coordinate and monitor the

strategy (e.g., data freezes, prioritization and monitoring of re-analysis projects, interpretation strategy, participating groups, and timelines, summarizing and reporting of results and findings), engage with other WPs (e.g., WP6, WP8, Data Services Hub) for data transfer, and align with B1+MG/GDI initiatives. T7.1. aligns with GO:1; SO:5; OO:2,3,5.

T7.2. Standardised exome and genome re-analysis beyond state-of-the-art diagnosis (M1-M84) TL: CNAG,CAD; Contributors: UT, SRUMC, UU, CENTOGENE, CHEO-RI*, UMCG, Inserm_Orphanet, CIBER. In Y1-3, standardized re-analysis of REAL data sets will be organized through distributed analysis, the RD-Connect GPAP and other platforms (coordinated via T7.1). In parallel, a federated model will be prepared, in collaboration with WP15, to ensure pipeline portability and implementation, and with those partners having capacity (INSERMCAD, UU). Federated analysis will be favoured as soon as operational and deployment aspects are resolved. The first 18M will focus on exome re-analysis, moving to srWGS, and LRS later (informed by WP8). Analyses will include all variant types, for which consensus algorithms are determined via 'Data Challenges'. Initially, focus will be on coding regions, shifting to non-coding regions on par with analysing genome REAL data. Variants will be transferred to DITFs (T7.3) for interpretation. T7.2. aligns with GO:1; SO:1,4,5; OO:1,3.

T7.3. Innovative exome and genome re-analysis (M7-M84) TL: SRUMC, ISCIII; Contributors: CHU Dijon, UGENT, UNEW*, CENTOGENE, RS(GMS-GMCK), GMS-RS, IMAGINE, CHEO-RI*. Interpretation of variants (from T7.2) will be coordinated by 3 super-DITFs for efficiency and uniformity across all disease groups/ERNs. Super-DITFs are responsible for multiple disease groups/ERNs, combined based on overlapping clinical spectra, or joined through national undiagnosed disease networks. Involvement of local HCPs is achieved via data submission (WP6) and yearly 'Solvathons' (years 2-6). First, we will focus on interpretation of existing genomic datasets, and the coding sequence, moving towards non-coding sequence with the availability of genome data and other -omics datasets (informed by WP8). In addition to analysis of known RD disease-genes, focus will include novel disease-gene/mechanism discovery. New diagnoses will be communicated to the patients via the local HCPs/submitters. T7.3. aligns with GO:1; SO:1,4,5; OO:4,5.

T7.4. Propagation of knowledge and best practice guidelines (M1-M84) TL: KU Leuven, INSERM_U974; Contributors: CAD, IBG, SRUMC, EURORDIS, CNAG. To shorten the pathway to diagnosis and to treatment, two translation tools will be targeted. First, a molecular diagnosis may provide (in)direct leads for therapeutic strategies in n=1 or n=few trials (link to WP12), requiring links with repositories to Treatabolome (link to WP16) and/or other actionable variants for immediate identification. We will provide implementation
guidelines to promote implementation in local health care services. Second, the usefulness of knowledge base and ontologies (WP16) will be promoted and evaluated for their performance in clinical context based on their yield. T7.4. aligns with GO:1; SO:1,2; OO:1.

Work package WP8 – Innovation to shorten time to RD diagnosis

Work Package Number	WP8	**Lead Beneficiary**	11 - SRUMC
Work Package Name	Innovation to shorten time to RD diagnosis		
Start Month	1	**End Month**	84

Objectives
To establish the most innovative diagnostic approaches for RD to enable a significantly shorter time to diagnosis by full genome analysis, omics integration, and interpretation. These innovations will be crucial to make more RD families amenable to actionability, therapy, and improved care. Several WP8 objectives can be later utilized by joint transnational calls. Specific objectives: (1) Enable complete long-read genome analysis for RD diagnoses as a truly generic and fully complete test; and (2) Develop new genomics and integrated multi-omics approaches to interpret genetic variation enabling improved RD diagnoses and that can be implemented across Europe.

Description
T8.1. Enable inclusion of underrepresented countries into innovative RD diagnostic research (M1-M48) TL: MUH, VULSK, Contributors: SRUMC, TUM, CNAG, UT. T8 will connect RD experts across Europe and let RD clinicians, scientists, and patients from underrepresented countries participate in the diagnostic innovations and train a RD-expert network in selecting RD patients for the T8.2-3 use cases. This capacity building (with WP20.3) leads to optimized RD case selection, increased and faster diagnoses. T8.1. aligns with GO:1; SO:1,2,4; OO:1-4. T8.2. Enable complete long-read genome sequencing and analysis for RD to shorten time to diagnosis (M1- M84) TL: SRUMC, UT; Contributors: UMCG, CHEO-RI*, TUM, CNAG. We will provide RD-optimized longread sequencing (LRS) pipelines. These shall be tested on selected use cases (Task 8.1) to assess diagnostic rate and time to diagnosis. Our LRS experts will analyse and interpret data jointly with disease experts. Innovations will lead to a truly complete and generic diagnostic test, with best practices translated across Europe. T8.2. aligns with GO:1; SO:1,2,4; OO:1-4. T8.3. Enable complete genome mapping for RD to shorten time to diagnosis (M13-M48) TL: SRUMC, UCL*; Contributors: TUM, CNAG, UT. As in T8.2, we will provide RD-optimized ultralong-read optical genome mapping (OGM) pipelines to the RD community, however, with a focus on other use cases, leading to more complete RD diagnostic tests, best practices, and translation across Europe. T8.3. aligns with GO:1; SO:1,2,4; OO:1-4. T8.4. New genomics (transcriptomics) analysis capabilities to understand genetic variation in RD (M1-M84) TL: TUM, CCRI GmbH; Contributors: CUH*, IBG, CNAG, SRUMC, UT. RNA-seq reveals aberrations in expression and splicing missed by genome analyses, leading to increased diagnostic rates and mechanistic insights. Together with national efforts, we will develop algorithms, interpretation guidelines, and interfaces to jointly analyse DNA and bulk and single-cell RNA data. It will include variant effect predictors with (sc)RNAseq-based tools and variant phasing from long-read sequencing. We will record diagnostic rates by aberration type and time each step from the first visit to diagnostic. T8.4. aligns with GO:1; SO:1,2,4; OO:1-4. T8.5. Multi-omics data integration to shorten time to diagnosis in RD (M13-M84) TL: TUM, AMU; Contributors: CCRI GmbH, OPBG, REGIONH, SRUMC, CNAG, UT. T8.1-4 focus on pinpointing the effects of variants on the gene they are located in. However, disease-causing variants can also affect in cascade the function of further genes. These consequences can be used to identify the culprit and understand disease mechanisms. T8.5 will do so by implementing new AI techniques integrating multiscale omics data layers and phenotypic data, with a focus on epigenomics. Every step, data modality, and analysis strategy will be monitored for time and diagnostic rate. T8.5. aligns with GO:1; SO:1,2,4; OO:1-4.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Work package WP9 – Real World Data

Work Package Number	WP9	Lead Beneficiary	13 - UKHD
Work Package Name	Real World Data		
Start Month	1	End Month	84

Objectives

To augment the trial readiness of real-world data available to the CRN partners. Specific objectives: (1) To develop an efficient system to retrieve primary healthcare data for RD outcome research; (2) To demonstrate the utilization of population-based data in RD outcome research; (3) To generate powerful reference patient cohorts by integration of heterogeneous data sources; (4) To collect and make available regulatory-grade natural history reference data; (5) To develop innovative models to predict disease progression in rare and ultrarare diseases; (6) To develop a platform for clinical trial simulation of RD populations. (7) To demonstrate the usefulness of the ERDERA Data and Expertise Hubs for enhancing the clinical trial readiness and scientific value of RD RWD.

Description

T9.1. Use of primary healthcare data for RD outcome research (M1-M60) TL: SRUMC; Contributors: VHIR, APHP, Erasmus MC, UPM, LMU, KUM. Structured and unstructured EHR data will be extracted and prepared for re-use in registries and outcome research projects. The following disease groups will be studied: Urogenital and craniofacial anomalies, neuromuscular disorders, epileptic encephalopathies, mitochondrial diseases, and rare anemias. Each subproject will involve EHRs at several HCPs, with different platforms (commercial and in-house) and different languages. Different solutions will be benchmarked on a common set of manually annotated EHRs in different languages. In parallel, we will demonstrate for each site how automated extraction from EHRs can be realized. This involves the following steps: (1) Obtain institutional approvals and data use conditions for EHR data extraction from HCPs; (2) Data pseudonymization and determining level of anonymity; (3) Compile structured and/or unstructured data items to be extracted; (4) Implement mappings to existing ontologies and semantic models, starting with common data elements (CDE), semantic model for CDEs and mappings to OMOP; and (5) Create structured output forms from unstructured text using NLP methods and evaluate their utility by clinical domain experts. T9.1. aligns with GO:2,3; SO:2,5; OO:1,2.
T9.2. Use of population-based data for RD outcome research (M1-48) TL: APHP; Contributor: Sciensano, UKHD. Innovative approaches to empower population-based outcome research will be developed in T9.2., including the development of a generic minimal interoperable dataset for population-based studies based on linked ERN and social security data. Three case studies will cover different care pathways, including one mostly surgical, one mostly based on successive drug regimens, and one based on neonatal screening: In ST1, exploring Dravet syndrome, the French National RD Registry (BNDMR), and National Health Data System (SNDS) will be combined with the Italian national Dravet registry to study the impact of drug therapies on life expectancy and healthcare costs. Both cohorts will be shared with the EpiCare registry. In ST2, national health insurance data of Hirschsprung disease patients will be linked with outcome data collected nationwide in Belgium, combined with equivalent national healthcare data from BNDMR and SNDS in France, analysed for the impact of phenotype and care pathways on health outcomes, and shared with the ERNICA registry. ST3 will develop a pathway for evaluation of the long-term impact of population-based newborn screening (NBS). A generic NBS module with controlled vocabularies and ontologies will be developed, enabling AI/ML data readiness. The module will be adapted for metabolic diseases and implemented in MetabERN's U-IMD registry, which contains longitudinal RWD from patients diagnosed either pre-symptomatically by NBS or after manifestation of symptoms. This will enable evaluation of NBS programmes across various screened diseases and EU countries and involve interactions with the Screen4Rare/ERN multistakeholder platform and ongoing EU initiatives towards genomic NBS (Screen4Care, NGS4NBS). T9.2. aligns with GO:3; SO:2; OO:2.
T9.3. Integration of patient cohorts for natural history/standard-of-care reference studies (M1-M60) TL: UKHD; Contributors: APHP, UT, LUMC, SRUMC. T9.3. aims to demonstrate the usefulness of the ERDERA Data Hub services to integrate existing RD registry data into large high-quality reference cohorts for future clinical trials. Four case studies will be performed: (1) Three regional registries from Italy, Germany and France will be joined with the ILIAD registry, and a national French cohort to create a single natural-history cohort of "RASopathies", a disease group for which molecular therapeutics are becoming available; (2) The international PodoNet Registry of >2,000 children with congenital and steroid resistant nephrotic syndrome will be integrated with the respective sub-cohort in the ERKReg Registry and local databases to form reference populations for emerging first-in-human gene therapy studies in monogenic podocytopathies; (3) Rare endocrine and bone disease cohorts followed in the EuRRECa/EURR-Bone registries will be pooled with institutional and national databases to generate reference outcome data for surgical

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interventions, e.g., in pituitary adenoma or osteogenesis imperfecta; (4) The TreatHSP (hereditary spastic paraplegia), PROSPAX (spastic ataxias) and ARCA (autosomal recessive cerebellar ataxia) registries will be integrated to >5,000 data sets including clinical information, digital mobility measures, molecular biomarkers, and genetic markers to develop advanced disease progression models (task 9.5) and patient-relevant outcome concepts (task 10.1). All integrated cohorts will be FAIRified, onboarded to the ERDERA Virtual Platform and made available in clinical-trial ready formats (tasks 9.4, 13.3, 14.2). The metadata of all cohorts will be deposited in ERDRI. A concept for future integration in the EHDS will be developed. T9.3. aligns with GO:1,3; SO:2; OO:2,3.

T9.4. Development of a blueprint and inventory of regulatory-grade natural history cohort data (M1-M84) TL: LMU, KUM; Contributors: UKHD, INSERM_U1112, C-Path. T9.4. aims to establish the procedures for academiadriven registries and cohort studies to achieve EMA qualification to serve as external comparator arms in CTs, post-authorisation safety surveillance and efficacy studies. For such EMA qualification, RWD must fulfil numerous requirements and must undergo extensive and iterative regulatory discussions. We plan to develop a procedural blueprint based on the exemplary processing of three European RD registries and cohort studies (on mitochondrial disorders, hereditary spastic paraparesis and C3 glomerulopathy). From these pilot projects, an inventory and point-by-point guidance will be developed, and comprehensive support provided for registries/cohort studies aiming to achieve regulatory-grade status. The project will be performed in collaboration with EMA's Data Analysis and Real-World Interrogation Network and coordinated with the IHI consortium for innovative RD therapies. T9.4. aligns with GO:2; SO:2; OO:2.

T9.5. Disease progression modelling and prognostic biomarker research (M13-M60) TL: UT; Contributors: VHIR, UPM, UKLFR, UKHD. T9.5. aligns with GO:2,3; SO:1,2; OO:1. T9.5. will develop and apply innovative RD progression modelling methodology in three paradigmatic disease groups: ST9.5.1. Focuses on spastic ataxia diseases (SPAX), a group of >300 ultrarare diseases which share progressive damage to the spinocerebellar and pyramidal tracts. Multimodal longitudinal outcome datasets established in task 9.3 will be utilized for disease progression modelling. An innovative statistical toolbox for individual and n-offew diseases course prediction based on clinical and biomarker profiles (digital-motor datasets, molecular and imaging biomarkers, genetic stratifiers) will be developed and validated.

ST9.5.2. Address sickle cell disease, aiming to develop individual risk models to improve disease characterization and health status monitoring, personalize therapeutic approaches and ultimately optimize health outcomes. Further to the longitudinal dataset of the rare anemia ERN registry with >600 variables covering clinical manifestations, organ damage, treatments, and laboratory data mapped in OMOP, multimodal information including metabolomic, genomic (SNP microarrays) and radiomic data (>500 cerebral MRIs) is available for analysis.

ST9.5.3. Explore spinal muscular atrophy, using the SMArtCARE registry with longitudinal data from >2000 patients treated with one of the three drugs approved for this disorder. This high-quality longitudinal dataset, which is part of the EURO-NMD registry hub and currently used for regulatory and HTA purposes, will be used to model SMA disease trajectories and to test the reproducibility of clinical trial results in a real-world setting. The projects will receive extensive support from ERDERA modelling experts (WP19). Prior EJP-RD work on individual disease prediction, quantification of uncertainty and simulation of treatment-induced deviations will be developed further towards multimodal outcome progression modelling and use for trial-readiness. The simulation of treatment-induced deviations from predicted individual progression trajectories for ultra-rare neurological diseases will set the stage for the innovative n-of-1 and n-of-few treatment trials envisaged in WP12.

T9.6. Development of a model-based clinical trial simulation platform for RDs (M7-M54) TL: C-Path; Contributors: DDF, UKHD. T9.6. will use existing and create new model-building technology to demonstrate the creation of Drug Development Tools (DDTs) that will improve the understanding of RD progression patterns and help predicting the effectiveness and safety of new drugs faster, with more certainty, and at lower costs. Natural history and previous clinical trial data will be used to develop prediction models that allow to simulate therapeutic intervention effects on clinical endpoints and trial sample size requirements, using both conventional and smallpopulation trial designs. Data modelling will be performed on the C-Path RDCA-DAP platform. A strategy for the formal review and potential regulatory endorsement of the quantitative and/or AI based disease progression models as DDTs will be developed. Two therapeutic areas have been selected for DDT development based on their advanced stage of regulatory milestone achievement and initial modelling experience: Duchenne Muscular Dystrophy (DMD) and Autosomal Dominant Polycystic Kidney Disease (ADPKD). The experience of DDF in novel machine learning (ML) methods and C-Path's expertise in developing quantitative solutions will be joined to generate an enhanced CTS tool for DMD. For ADPKD, ERKNet with its registry cohort of >3,000 patients, CPath and the US PKD Outcomes Consortium will undertake a transcontinental collaboration to develop a globally applicable PKD progression model towards regulatory maturity as a DDT. Based on the modelling expertise generated in the ADPKD project, modelling of the eGFR loss endpoint will be considered also for other progressive rare kidney diseases with a therapeutic perspective (e.g. SRNS, IGA nephropathy, complement mediated diseases) for which high-quality RWD is available. T9.6. aligns with GO:2; SO:2; OO:1,2.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Work package WP10 – Clinical Outcome Assessment

Work Package Number	WP10	Lead Beneficiary	15 - VHIR
Work Package Name	Clinical Outcome Assessment		
Start Month	1	End Month	84

Objectives
WP10 aims to promote the development and integration of PCOMs (PROMs and other COA types) together with PREMs and socioeconomic information for monitoring clinical research (CTs, clinical studies, patient registries) and assess its efficacy and safety for patients together with the evaluation of disease progression: (1) To develop a platform for the development and validation of regulatory-grade PCOMs for RDs which are suitable for establishing truly patient-centred clinical trial endpoints, based on core disease/group of diseases impact sets on the patient as well as societal level; (2) To develop and implement digital tools allowing efficient and broad collection of PCOMs patient self-reported data (PROMs/PREMs, socio-economic information etc) in RD patient cohorts and integration with patient databases and research data; and (3) To systematically explore the societal impact and personal burden of RDs across Europe.

Description
T10.1. Platform for regulatory-grade patient-centred COA development and validation (M1-M84) TL: UKHD; Contributors: VHIR, LMU, KUM, UT, APHP, Erasmus MC, MRT, EURORDIS. In a multistakeholder patient-centred process, we will develop patient-reported outcome assessments and assess patient-relevance of top-ranked COA candidates for five demonstrator RDs (HSP/ataxia [ERN-RND], RASopathies [ERN-Ithaca], mitochondrial disease [5 ERNs], rare anemia disorders [ERN-EuroBloodNet], and craniofacial anomalies [ERN CRANIO]. We will: (1) establish ICF-coded core impact sets for each of the RDs, (2) match ICF-coded functional impacts with suitable existing PROMs (Coll ERICA), and (3) validate PROMs in at least 3 European languages, establishing sensitivity to change, meaningful within-patient change and crosslanguage equivalence. Additionally, anchoring studies for top-ranked COA candidates in the four demonstrator diseases will be performed to establish their patient-relevance. T10.1. aligns with GO:2,3; SO:1-4; OO:1,4,5. T10.2. Development and Implementation of Clinical Outcome Assessment Tools (M1-M84) TL: VHIR; Contributors: UT, APHP, UKHD, UPM, EURORDIS. In T10.2., methodologies to collect and implement PCOMs data linked to patient registries will be developed, considering legal, technological, and regulatory requirements, and validated in 4 case studies using mobile health solutions and devices on rare neurological, neuromuscular, kidney, and haematological disorders. (1) Development of study protocols including the collection of end-user clinical and technical requirement and data standardization (Coll WP13); (2) Identification of available mobile Apps and devices and their readiness (Coll WP14); (3) Clarification of regulatory aspects: mHealth privacy and security protections (Coll WP18); (4) Development/ adaptation of mHealth solutions linked to patient registries; (5) Clinical studies execution; (6) Validation of patient generated data for data quality; and (7) Development of a data visualization framework. T10.2. aligns with GO:2,3; SO:1-4; OO:1,2,5. T10.3. Unveiling the Hidden Burden: Estimating the Socioeconomic Impact of RDs for Informed Decision Making and Resource Allocation (M13-M72) TL: Sciensano; Contributors: Erasmus MC, RDI, EURORDIS, APHP, WDO, CVBF, QUB-UK*. T10.3. will establish and implement a framework for estimating the socioeconomic impact of RDs in Europe based on real-world data through data mapping, Disability Adjusted Life Years (DALY) calculation, and cost estimation in ten RDs and related available registries. 1) Protocol based on harmonized and improved methods for calculating RD DALYs. It will include consensus disease models, outlining the key health states and Disability Weights. 2) Protocol based on harmonized and improved methods for calculating Cost of Illness (COI) associated with RDs, including caregivers. It includes assessing direct medical costs and assessing indirect costs by monetizing Years of Life Lost (YLL). Protocols will include methods to visualize the impact of different scenarios, e.g. impact of new treatment on the DALY and COI estimates. A dedicated stakeholder strategy targeting patient registries owners will foster uptake at national level, aiming for routine quantification of the socioeconomic impact of RDs. T10.3. aligns with GO:2,3; SO:3,4; OO:1,4,5.

Work package WP11 – ATMPs

Work Package Number	WP11	Lead Beneficiary	1 - INSERM

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Work Package Name	ATMPs		
Start Month	1	End Month	84

Objectives

To demonstrate the applications of established innovative, scalable technology platforms of ATMPs developed in the Acceleration hub for prioritized RDs. This WP will collaborate with the two WPs that focus on diagnosis and natural history studies, which are essential for therapy development. In the first year of the project, the objective will be to identify the most urgent and suitable disease groups for ATMP therapies. For following years, objectives will be: (1) To match technology platforms to diseases with greatest need for and benefit from ATMPs; (2) To design proof of concept studies to pressure test selected technology platforms; (3) To assess readiness to enter a clinical development based on available data and technology platform; and (4) To promote ATMP clinical development by establishing a network of qualified clinical trial sites.

Description

T11.1. Identify and rank disease indications requiring ATMPs (M1-M12) TL: UKHD; Contributors: EURORDIS, CVBF. A multistakeholder survey will be performed across the ERDERA. First, general criteria for ATMP treatment suitability will be pre-defined by experts. The main parameters and relative weight in the algorithm will include disease demographics, morbidity/disability, potential for therapeutic efficacy based on mechanistic considerations, availability of established intervention endpoints, natural history studies, efficacy and
safety of current therapies, availability of European study cohorts. Priority lists of suitable candidate conditions will be generated, and the most promising candidates will be chosen for demonstrator projects. From the collected information, priority lists of suitable candidate conditions with the greatest anticipated potential benefit from ATMP therapies will be derived for each ATMP class and the most promising candidates will be chosen for demonstrator projects. T11.1. aligns with GO:2; SO:1,2,4,5.
T.11.2. Select and adapt the technical platforms with prioritised need (M12-M36) TL: GNT; Contributors: Inserm_ART-ARNm, Pfizer*. Technical platforms with high performance identified among those developed in WP21 will be selected to meet the requirements for the disease list developed in T11.1. The ATMPs experts committee including multiple stakeholders created during T11.2 will prioritize the disease list, minimize the risks associated to the project implementation and identify three diseases for proof of concept. The criteria used for disease selection and the different views brought from the members of the selection committee will be used for the development of a specific algorithm based on AI (fitting gene sequence, gene size, organ/cell type and type of genetic modification and delivery system) that will help the future generations in such prioritisation strategies. T11.2. aligns with GO:2; SO:1,4; OO:2.
T11.3. Design the proof-of-concept studies to evaluate the selected pipelines (M36-M72) TL: INSERM_ART-ARNm, INSERM_IT-GGB; Contributors: FHG, GNT. Proof of concept studies will be designed to test the available technology platforms identified in T.11.2 on disease prioritized in T11.1. Human-based disease models of high clinical biomimicry including patient-specific disease models will be privileged whenever available. In case of metabolic diseases, the objective is to evaluate the efficacy of liver targeting in the presence of an underlying diseases, e.g., fatty or fibrotic liver so to better resemble the conditions encountered in western countries. Neurological disorders requiring central nervous system, muscle or dual CNS/muscle targeting represents the current frontier of gene transfer will be a second target. Technologies targeting HSCs after systemic delivery will allow for gene replacement and gene editing thus addressing a large part of rare genetic diseases. The task will be performed with a close interaction between the Accelerator hub and clinical development partners to better implement the clinical translation. T11.3. aligns with GO:2; SO:1,4; OO:2.
T11.4. Evaluate the selected platforms for CTs requirement and joint transnational call (M48-M84) Contributors: CVBF, UC, GNT, INSERM_ART-ARNm. The most effective combinations of innovative ATMP and RD in terms of therapeutic efficacy as well as manufacturing capacity and cost-effectiveness will be selected for CTs by a dedicated Committee of ATMP expert (M36-72) and incorporate inputs from experts in WP21 Innovative Therapies Technology Accelerator. Criteria and assets for the selection of platforms/disease combination will be:
(1) The possibility to scale-out to GMP manufacturing of the Innovative ATMP; (2) Existence of sufficient data for the authorization of a Clinical Trial Application including a proof-of-concept in an accepted disease model; (3) A positive risk/benefit assessment for the patients; and (4) The existence of a clinical network able to perform the clinical trial with access to the required patients. To this end, we will be launching internal call for partnership to build a regulatory and clinical network supporting pre-IND studies (M24-48). ATMP based CTs will be funded through the JTCs within the WP11 based on the priorities identified in Task 11.1 and the technology readiness assessed by the ATMPs experts' committee. In addition, based on the advancement status of the preclinical phase, support to identify alternative fundings for the clinical translation will be provided by the WP11 and the Acceleration Hub. T11.4. aligns with GO:2; SO:1,4; OO:2,3.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Work package WP12 – N-of-few Approach

Work Package Number	WP12	Lead Beneficiary	16 - LUMC
Work Package Name	N-of-few Approach		
Start Month	1	End Month	84

Objectives
(1) Develop an academic platform to develop and test tailored antisense oligonucleotide treatments; and (2) Four use cases to pressure test the platform.

Description
T12.1. Academic platform development (M1-84) TL: LUMC; Contributors: UKHD, UT, SRUMC, UKLFR, WDO, RCC*. T12.1. aims to establish an innovative, scalable platform for academic development and implementation of mutation-specific antisense oligonucleotide (ASO) treatments for individuals with nanorare RD mutations. Along this pipeline will create a combined preclinical/clinical/regulatory framework for tailored n-of-1/n-of-few treatments; and implement, standardize, and optimize each of its modules, processes, and levels. The platform will cover the following aspects: (1) Patient identification (link to diagnostic registries in ERNs and treatment board); (2) ASO design and synthesis (consensus on processes); (3) Efficacy assessment (consensus on processes); (4) Toxicity and safety assessment (consensus on process and reducing the need of animals); (5) Identification of patient relevant outcomes in an n-of-few setting and run-in natural history studies (task 12.2); (6) Treatment/study design and analysis (task 12.3); (7) A registry to capture individualized patient relevant efficacy and safety outcomes before and after treatment; (8) Implementation of first in human treatment infrastructure in n-of-few setting (task 12.4); (9) Regulatory; and (10) Ethical framework (built from pieces generated for each of the aspects. In M1-36, we will build the components of the platform and roll out to one underrepresented country. In M37-84, we will roll out the platform across other centres that will treat patients with individualized therapies and iteratively optimize components based on feedback from the case studies (T12.5) and participating centres. T12.1. aligns with GO:1; SO:1; OO:3,5. T12.2. Identification of patient relevant-outcomes (n-of-1/few) and run in natural history study (M1-84) TL: UT; Contributors: UKHD, LUMC, FSJD-CERCA. T12.2. aims to (1) Develop adapted processes for patient-relevant outcome selection (CRN – Outcome Research) to fit the n-of-1/n-of-few setting; (2) Identify a toolbox of diseasespecific and generic outcomes coordinated by the WP manager during consensus multistakeholder meetings including participants from across Europe (at least 35% underrepresented countries); (3) Implement run-in natural history studies to determine individual sensitivity to change of candidate outcomes selected by patient and clinician and pre-treatment progression trajectories. T12.2. aligns with GO:2; SO:1; OO:3,5. T12.3. Treatment/study design and analysis (M1-84) TL: UT; Contributors: UKHD, UKLFR, LUMC. T12.3. aims to (1) Achieve consensus on strategies to evaluate treatment efficacy on an n-of-1 level (e.g., implementation of staged evaluation milestones: safety – target engagement – efficacy on surrogate parameters – clinical efficacy); and (2) Develop platform trial design that allow to assess efficacy of the platform approach across diseases and treatments, coordinated by the WP manager. T12.3. aligns with GO:2; SO:1; OO:3,5. T12.4. Implementation of first in human treatment infrastructure (M1-84) TL: UKHD; Contributors: UT, LUMC. T12.4. aims to (1) Develop criteria and a process for site qualification; and (2) establish a network of qualified of clinical sites in European countries that can carry out n-of-1 treatments. Criteria will be set, and pressure tested by first use cases by centres with lead experience in implementing this human treatment infrastructure (see Task 12.5) and during consensus meetings, coordinated by the WP manager. The infrastructure will be rolled out to the first underrepresented country in M1-36. T12.4. aligns with GO:2; SO:1; OO:3,5. T12.5. Case studies (M13-M84) TL: UT, UKHD; Contributor: LUMC. The power of the platform generated in Task 12.1 will be shown by 4 use cases, selected to represent different challenging scenarios (e.g. n-of-1; n-of-few; childhood/adult onset; target tissue e.g. brain/eye/liver) to pressure test the platform. We will start with 2 use cases using ASOs for ataxia telangiectasia and POL3RA-related neurodegeneration in M13-36. In M50-84, 2 other use cases will be selected from within the network. These use cases can be either ASOs (using the whole platform) or ATMPs (using aspect 5-9 of the platform). Selection will be facilitated by the selection criteria set in the treatment board (task 12.1) and in collaboration with WP21. Note that for each use case a contribution towards development costs will be provided. T12.5. aligns with GO:2; SO:5; OO:1,3.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Work package WP13 – RD Virtual Platform (RD-VP) finding and accessing the data ecosystem

Work Package Number	WP13	Lead Beneficiary	1 - INSERM
Work Package Name	RD Virtual Platform (RD-VP) finding and accessing the data ecosystem		
Start Month	1	End Month	84

Objectives
(1) To scale up the federated infrastructure built in EJP RD (RD-VP) by evolving a service-oriented architecture (SOA) in which data, knowledge, and analysis methods from CRN/JTC/CT projects can contribute to the ERDERA data hub as value proposition, at annually increasing rates: To expand the adoption of semantic and technical standards to new sources of data, in order to increase the interoperability and usefulness of the ecosystem for RD research (VP compliance); to steer the expansion (make new resources, including CRN/JTC/CT results, automatically findable within the SOA-based ecosystem) and reusability (allow for querying and reusing data within the connected resources) of the ecosystem in relation to ERDERA workstreams needs, and to support their development; (2) To 40organize and technically lead the teams of Data Hub + CRN/JTC/CT researchers and developers to effectively complete projects that result in increasing numbers of stakeholders contributing to the Data Hub as value proposition (effectuate the CTO role); (3) To support WP14-16 in their collaborations with projects contributing data, analysis, and knowledge to the ERDERA data hub as value proposition; and (4) To ensure the interactions with other ecosystems in Europe and at the international level as far as they respond to ERDERA needs. This WP impacts all GO:1-3; SO:1-5; OO2.

Description
T13.1. VP/data service hub steering (M1-M84) TL: INSERM_Orphanet; Contributors: LUMC;AUMC, UTWENTE, Pfizer*, ROCHE*. Data Service Hub Task leaders, CRNs WS leaders, Funding research WS leaders, National and international alignment WS leaders. The extension and evolution of the RD VP will follow a steering and prioritization process, at the strategic and operational level. The VP is expected to evolve into an intelligent learning system in which newly added resources contribute to statistical, AI, and ML applications. The strategic prioritization of the DSH activities will be done in cooperation with the global ERDERA strategy (task 1.2), to ensure that developments and services in the DSH remain aligned with the SRIA specific objectives, and with the ERDERA overarching prioritization. Special attention will be given to the cooperation with other European and international initiatives. Crosstalk with the ERDERA ELSI, IPR and regulatory services in relation to aspects relevant for the VP will be ensured. The operational decision-making process will be designed according to Agile methods in monthly development cycles. T13.1. aligns with GO:1-3; SO:1-5; OO:2. T13.2. RD-VP evolution and scaling up (M1-M84) TL: UTWENTE, AIT; Contributors: INSERM_Orphanet, BBMRI-ERIC, UPM, GUF, UMCG, LUMC, ULEIC*, CNAG, UKLFR, QUB-UK*. This task has two main responsibilities: (1) Maintain and evolve the RD-VP's architecture and specifications, and (2) Overlook the developments to guarantee that they conform with the VP's architecture. T13.2. main activities include: (1) Curation and evolution of the Virtual Platform's architecture and specifications in collaboration with all involved partners and Tasks 13.1 and 13.3; and (2) Overarching technical developments management of the Virtual Platform to guarantee compliance of the developments with the VP's architecture and specifications in collaboration with the stakeholders responsible for the developments. Service-oriented evolution of components, including VP Index evolutive maintenance, metadata and data models updates, AAI and consent, PPRL interoperability, core Orphanet services, content discovery services based on Beacon framework, distributed analysis services and VP Portal. T13.2. aligns with GO:1-3; SO:1-5; OO:2. T13.3. VP onboarding services (M1-M84) TL: UMCG, UPM; Participants: SRUMC, LUMC, AUMC. T13.3. is responsible for the maintenance and evolution of the onboarding documentation, services, operations, and support. Based on the steering and prioritization of new resources to be connected to the RD-VP conducted by Task 13.1, Task 13.3 engages with these resources to offer support for the onboarding process, including automation approaches. Onboarding of these resources will track closely with the requirements of WP14 and WP15, to aid in the rapid establishment of analytical pipelines through improved resource discovery. T13.3 will implement practical tools, scripts, and templates to expediate the onboarding process, using ERDERA prioritized software platforms and standards, including assistance with hosting of connected services where needed, providing documentation/SOPs, a support channel and sessions into ERDERA training WPs. Attention will be given to the appropriate capture of legal and IP expectations and constraints, in relation with Task 1.6 – ELSI support service and WP18 Regulatory Support Service, to ensure proper usage, and credit, of the onboarded resources. The onboarding task will closely interact with the mentoring and consultancy service that integrates all ERDERA components and is designed to scale with the number of projects funded through JTC/CT

and CRN projects. In a direct feedback loop the consultancy will apply onboarding services for new resource types and provide feedback for their evolution. Conversely, the added value of onboarding will be directly demonstrable by analyses that run on onboarded resources. T13.3. aligns with GO:1-3; SO:1-5; OO:2.

Work package WP14 – Data readiness services

Work Package Number	WP14	Lead Beneficiary	16 - LUMC
Work Package Name	Data readiness services		
Start Month	1	End Month	84

Objectives

To expand the use of services by which RD partners contribute to ERDERA's robust infrastructure of data, resources, and expertise (SRIA OO2) to accelerate the automated ethical and legal exploitation of the healthcare and research data from their projects (based on guidance from WP1 and WP17-19), boosting scientific and regulatory evaluation and healthcare delivery (SRIA SO2). Specific objectives are: (1) To provide a workflow for RD partners to efficiently organise interdisciplinary data readiness teams executing FAIR data creation and
FAIR data processing customised to their project, accelerating the expansion of the ERDERA-Data Hub and supporting in-project analysis, federated learning and AI across projects; (2) To provide tools, semantic data models, and specifications that enable RD partners to make data records that they manage ready for automated use if and when accessed, and where needed initiate and monitor the development of missing tools, models and specifications. The enrichment resulting from WP14 pertains to machine actionability and interoperability of data records. The container of the records (e.g. a database or catalogue) must also be FAIR for the records to be findable, accessible, and reusable within the VP (see WP13); (3) To provide tools and services for RD partners to prepare data for the regulatory pathway in drug development, in collaboration with WP9 and WP18; and (4) To contribute to the design and privacy-preserving use of personal data that guarantees that individuals can access data records derived from them, be informed of derivate use of their data, data use conditions can be set at record or subset level, and partitioned data from the same individual can be linked.

Description

T14.1. Services for making data findable, accessible, interoperable, reusable for automated applications (M1-M84) TL: SRUMC, AUMC; Contributors: LUMC, UTWENTE, UPM, WDO, ISS, CNAG, FGB. T14.1. focuses on providing a working model by which RD partners can increase the exploitability of the data that they manage for their project, and for ERDERA, focusing on accelerating the adoption of instructions and tools (T14.2, T14.3) by the ERDERA projects, complying the strategic objectives of the ERDERA (e.g. SRIA SO2 and the GOs it
serves) and in collaboration with NMGs. Following a landscape analysis, it helps organise co-creation teams and workshops, via which a data readiness plan is made and executed. The results are tested by the ERDERA projects, and stakeholders proving that the ERDERA-DH serves multiple stakeholders. The role of PLWRD in viewing and managing their own data is monitored. T14.1. aligns with GO:1-3; SO:2,4,5; OO:1-5.
T14.2. Data ingestion tools (M1-M84) TL: UMCG, UPM; Contributors: AUMC, LUMC, SRUMC, AIT, CNAG, CRG-CERCA. T14.2. focuses on providing generic tools that the data readiness teams use to accelerate the usability of data. Data are made usable for responsible federated analysis on connected computing and analysis facilities. It builds on tools and standards previously developed, such as by Solve-RD and the EJP RD. They in turn have built on international collaborations and European projects that investigated implementation of FAIR data principles. Tools for making data ready are identified and developed by co-creation teams, populating the ERDERA-DH. It achieves two goals: (i) make data from CRN/funded projects more exploitable, (ii) evolve data ingestion tools for the ERDERA-DH, particularly focusing on scalability. T14.2. aligns with GO:3; SO:1-3,5; OO:1-3,5.
T14.3. Services for advancing the regulatory pathway in drug development (M1-M84) TL: C-PATH, DDF; Contributors: WDO, LUMC. Projects at all stages of the development need to contribute to regulatory approvals to address the unmet medical needs of the RD community in a timely manner and in a way that is meaningful to patients. The development of existing and new predictive tools and methods that qualify as Drug Development Tools (DDTs) require regulatory and data science strategies at design and planning stage to accelerate innovation and the use of Real-World Evidence (RWE) in study design and medicines developments. This task maximises the use of data by tools, accessible to the community, for optimising and accelerating drug development for RDs. The C-Path Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP®) serves as an accelerator and target platform. It contributes best practices to

scale up the usability of RD data in the regulatory process (WP9, WP17, WP18). It connects to the patient and regulatory community through the patient advocacy groups of UPPMD and DDF. T14.3. aligns with GO:2; SO:2,4,5; OO:1-5.

Work package WP15 – Data sharing and analysis services

Work Package Number	WP15	Lead Beneficiary	19 - UMCG
Work Package Name	Data sharing and analysis services		
Start Month	1	End Month	84

Objectives
(1) Provide analysis ready reference deployments of the ERDERA analysis infrastructure, including support and interoperability with WP13-14 with ability to scale to cloud; (2) Provide protocols, software and pipelines for large data sets and high-performance computing (HPC) analyses to the infrastructure; and (3) Provide protocols, software and systems that enable federated data analysis use cases and pilots.

Description
T15.1. Data analysis platform deployment (M1-M84) TL: UMCG, ULEIC*; Contributor: CNAG, AIT. T15.1. aims to deliver ready to use analysis infrastructure, integrating output of T15.2-3 and key resources, i.e., high performance compute 'cloud' from EJP-RD, Solve-RD, CINECA, EOSC-life; federated analysis by Genomed4All, EUCAN-connect/ DataSHIELD; and user facing analysis services such as the RD-Connect GPAP and MOLGENIS. The infrastructure consists of portable and interoperable packages that can be installed and scaled-up by ERDERA partners on-site or on external (cloud) providers, including a system to track data, metadata, analyses, and the genomic variants interpretation workflow. T15.1. aligns with GO:1-3; SO:1,2,4,5; OO:1-5. T15.2. High performance compute pipeline and 'cloud' services (M1-M84) TL: UMCG, CAD; Contributor: CNAG. T15.2. aims to integrate and maintain best practice analysis pipelines that require 'high performance' such as genomics, AI and radiomics, building on key resources from RD-Connect GPAP/CNAG, MOLGENIS/UMCG VIP, PFMG2025, Clinical Genomics Sweden, and analysis services such as C-PATH and Orphascape-phenotypic (see task 15.3), and aligned with EOSC, EHDS and ESFRI developments (e.g. LS AAI via GDI project). Main work is to integrate methods prioritized by CRN and funded projects into portable and interoperable HPC analysis pipelines, bundled in a 'HPC' in a box template ('starter kit') to be installed by research partners to enable first distributed and later federated analysis between the ERDERA partners. T15.2. aligns with GO:1-3; SO:1,2,4,5; OO:1-5. T15.3. Federated analysis (M1-M84) TL: UPM, UU, CNAG; Contributor: UMCG, CAD, AIT, IMAGINE, CHEO-RI*. T15.3. aims to upscale the analysis infrastructure in a federated fashion, leveraging infrastructure from 1+MG/GDI and enabling distributed deployment of T15.1 and T15.2 assets to enable use cases and pilots in Subtask 15.3.1 (Federated analysis and federated learning infrastructure) and Subtask 15.3.2 (Technical support for international federated genome-phenome analysis for research) to realize intra-European and cross-continental analysis capability, starting with large datasets relevant to CRN and JTC projects, aiming to a sustainable approach. T15.3. aligns with GO:1-3; SO:1,2,4,5; OO:1-5.

Work package WP16 – Knowledge bases and ontologies for RD research

Work Package Number	WP16	Lead Beneficiary	20 - AUMC
Work Package Name	Knowledge bases and ontologies for RD research		
Start Month	1	End Month	84

Objectives
(1) Ensure the evolution, harmonisation, extend and adaptation of pre-existing knowledge repositories and ontologies; (2) Address the developing needs of RD researchers and clinicians regarding the use of knowledge resources; (3) Fill identified gaps in knowledge bases; and (4) Demonstrate the utilisation of these resources in supporting diagnosis and treatment research. This WP encompasses the following components: (1) PCOMs repository deployment; (2) Knowledge

base of prenatal phenotypic features of RDs for early diagnosis; (3) System linking molecular diagnosis to treatment (Treatabolome and RD maps); (4) RD maps – multidimensional knowledge networks – spanning from genetic causes to observed phenotypes and treatment pathways; (5) Ontology of functional impacts of RDs; and (6) HOOM (HPO-ORDO Ontological Module). Orphanet Functional Consequences Ontology (OFCO) covers various aspects related to RDs: (1) Incorporates ontologies like ORDO and HPO used in the RD domain; (2) Includes semantic models such as the EJP-RD semantic model; and (3) Integrates enriched versions of models like OMOP-CDM and CDISC. All resources are linked to the VP and to WS and WPs throughout the ERDERA: (1) Integrated use cases are demonstrated; (2) Tutorials and training offered; and (3) Made accessible for CRNs and funded projects in the form of services and collaborations.

Description

T16.1. Evolving a repository of FAIR Patient-Cantered Outcome Measures (PCOMs)/ Patient-Reported Outcome Measures (PROMs) (M1-M84) TL: INSERM_Orphanet, MRT; Contributor: AUMC. T16.1. aims to expand the PCOMs repository for RD developed in ERICA following the expansion of the annotations of functional impacts of RD performed by Orphanet in collaboration with patient organisations and RD experts, by statistically clustering RD around their functional impacts, to allow for repurposing of existing PCOMs. WP10 will use this repository for PCOMs validation and will feed this repository with newly validated PCOMs. Clustering will be facilitated by the creation of an ontology of functional impacts of RD in T16.5. T16.1. aligns with GO:3; SO:1-3; OO:1.

T16.2. Antenatal echographic and pathologic RD phenotypes knowledge base and ontology (M1-M84) TL: INSERM_Orphanet, Sonio. T16.2. aims to leverage on the knowledge being generated by the software and AI for prenatal diagnosis of RDs developed by Sonio, based on academic foetal medicine research, and to create a reference ontology of phenotypic annotations corresponding to detectable RD antenatal abnormalities, by proposing an extension of the HPO and Orphanet content (HOOM), in collaboration with foetal medicine and RD experts. This innovative, openly reusable content will allow for its integration into diagnostic pipelines for early detection and action-taking on RD, including guiding early genetic diagnosis, in the frame of CRN Diagnostics. T16.2. aligns with GO:1; SO:2; OO:1.

T.16.3. Treatabolome (M1-M84) TL: CNAG, INSERM_U974. The Treatabolome (http://treatabolome.org/) is a unique, FAIR, resource initially developed in Solve-RD that provides evidence-based links from genes and variants to published treatments with the objective that clinicians diagnosing patients can more easily find the published evidence they need to make appropriate treatment decisions for their newly diagnosed patients. The Treatabolome is encoded using ontologies and standards and the information is available through a user-friendly interface and an API to provide interoperability with other tools such as clinical decision support software. This task will engage with the ERNs to seek expertise on new disease groups and will develop a system to facilitate the entry of new data through literature mining and the curation and update of knowledge through a crowd-sourcing approach. T16.3. aligns with GO:2; SO:1-3; OO:2.

T16.4. RD maps (M1-M84) TL: UM, LUMC; Contributor: AMU. T16.4. is dedicated to building tools and services around RD maps connecting essential knowledgebases with each other, to provide models for identification and prioritization of biomarkers for diagnosis and treatment. These RD maps are multi-dimensional models of RDs, starting from molecular interactions – molecular machine-readable pathways developed in previously EJP RD – and connect with established and newly developed knowledgebases from Task 1, 2 and 3 for
phenotype and genotype connections and will be annotated with RD ontologies from T5. Additionally, the RD maps will support concrete research questions within the CRNs and funded projects. Within the project we will identify several concrete questions to solve using the RD maps and provide workflows and demonstrators how to create and analyse them, e.g. for ATMP or drug prioritization. The goal for the first 3 years is to establish workflows and interoperability between the resources in how to create the maps, the next 4 years are used for identifying and solving concrete research questions together with the CRNs and “ready” data from WP14 and WP9. T16.4. aligns with GO:1-2; SO:1,2; OO:2.

T16.5. Improving, creating, and expanding RD Ontologies and semantic models (M1-M84) TL: AUMC, INSERM_Orphanet; Contributor: LUMC, UM. T16.5. aims to contribute semantically enriched information models and ontologies to the graph-based repository emerging from this WP. On the one hand, existing RD ontologies will be enhanced to allow for better integration with other data into knowledge models, and novel ontologies will be created (antenatal phenotypes of D, T16.2., and functional impact of RD) and integrated with the Orphanet RD ontology (ORDO). On the other hand, semantic models for disease-specific data elements, including PCOMs elements, will be extended or developed, and semantic version of standard information models, including CDISC, OMOP-CDM, and Phenopackets, will be produced. These standardised reference data will be reusable in the frame of CRNs and JTCs research, as well as by Data readiness (WP14) and Data analysis (WP16) activities. T16.5. aligns with GO:1; SO:1,2,5; OO:2.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Work package WP17 – Mentoring and consultancy

Work Package Number	WP17	Lead Beneficiary	22 - EATRIS
Work Package Name	Mentoring and consultancy		
Start Month	1	End Month	84

Objectives
(1) Continue and further expand the successful EJP RD mentoring programme; (2) Mentoring will be implemented as an ERDERA strategy for projects funded by the alliance (WP3 and WP4) starting at the design phase and throughout the entire life of the project. By adopting the successful light-touch mentoring support scheme from EJP RD, research teams of the funded projects will benefit from a low threshold assessment of the critical milestones that are key for a successful translational development with the objective of reaching the clinic as soon as possible; (3) Perform a feasibility study of a potential workflow of additional expert support based on a consultancy services-based model. This study will analyse the long-term sustainability for this potential service provision. The assessment of this study will be determinant for including this additional service workflow in ERDERA; and (4) Provide feedback to ERDERA partners on the critical barriers for project progression based on the interaction with the research teams and recommendations for profiling the scope of the funding calls.

Description
T17.1. Execution of the Mentoring Program (M1-M84) TL: EATRIS; Contributors: FGB, VHIR. Coordinated and managed by EATRIS, mentoring support will be provided to eligible applicants of the funded projects (WP3 and WP4), who will be informed of the opportunity in the call text of the project calls, as well as through dissemination activities, such as webinars and presentations at suitable meetings and conferences. Selected projects will be offered the support of a dedicated Mentor (or mentors) who will utilize the Innovation Management Toolbox created in EJP RD and the EATRIS database of mentoring experts (also including experts from the partners involved in ERDERA and other institutions (including but not limited to ECRIN, CBVF, c4c, AFM Telethon and ISCIII. Experts will be trained in the mentoring workflow and a comprehensive database will be updated and maintained to cover all the expertise of the RD research value chain. Periodic reports of the mentoring activity will be generated that will be the base for the self-assessment of the process and establish the rationale for eventual adaptations of both at the strategic and operational levels. The mentoring process will also identify potential knowledge and methodology gaps that may require consultancy and/or methodological support. The outcome of the process will be periodic reports of the mentoring activity that will be the base for the self-assessment of the process and establish the rationale for eventual adaptations on both strategic and operational levels. T17.1. aligns with GO:1,2; SO:2,4; OO:2. T17.2. Consultancy service (M1-M84) TL: FGB; Contributor: EATRIS, VHIR. With the aim of providing the best support to the development of projects funded by ERDERA, and in general to the RD community, FGB will lead, during the first funding cycle, a task with the aim of exploring the need and the interest of providing additional expert support in the framework of a consultancy-based support service. Direct feedback from the mentoring service, as well as surveys and interviews with RD research teams will be the basis for a feasibility study that will assess the interest of creating a consultancy-based service as an additional workflow in ERDERA activities. This study will analyse the priorities, workflows, and financial sustainability of these potential service provision approach. A pilot test for assessing the efficiency and implementation of consultancy services will be conducted by FGB during the second funding and identify the feasibility of its implementation (including operational and financial considerations) as an additional service of ERDERA. This task will be developed in 2 subtasks. T17.2. aligns with GO:1,2; SO:4; OO:2.

Work package WP18 – Regulatory support service

Work Package Number	WP18	Lead Beneficiary	23 - FGB
Work Package Name	Regulatory support service		
Start Month	1	End Month	84

Objectives
To provide beneficiaries with a multi-specialistic regulatory support service, ensuring that consortiumderived tools,

methods, data, and sources are in line with up-to-dated requirements for regulatory filings including qualification. Specific objectives are: (1) To create a dedicated project Regulatory Support Group; (2) To develop new regulatory support tools outlined in tasks 18.1 and 18.2 to facilitate more effective translation of new therapies to the clinic; (3) To provide advice on opportunities, strategy, and timings to engage with regulatory agencies at the appropriate time during the project; (4) To facilitate the applications for regulatory procedures to regulatory procedures to the European Medicines Agency (EMA) or other regulatory bodies; and (5) To support efficient, regulatory-compliant first in man CTs. Regulatory support will be also delivered to researchers from funded projects
through consultancy services (Task 17.2).

Description
T18.1. Regulatory support to preclinical research (M1-M84) TL: EATRIS, IABS-EU, Miltenyi*; Contributors: Pfizer*, RJF*, AZ*, UCB*, HIPRA*, LAB HIPRA*, ROCHE*, FDB*. A one stop point to support preclinical research to develop therapeutics, including ATMPs, for RD, in addition to the support outlined in task 18.2 will be created, to facilitate a more accessible regulatory process by helping to implement new standards and tools that help developers meet regulatory requirements early on. To this aim, this ERDERA regulatory support group will: (1) Facilitate successful delivery and qualification of new tools and methodologies, appropriate resources, and databases that support efficient ATMP development for RD; (2) Assess current Pharmacopeia chapters/monographs related to ATMPs for RD for relevance and recommend necessary additions and modifications to be implemented based on the technology platforms and new data generated within ERDERA and beyond, through close interaction with the European Directorate for the Quality of Medicines & Health Care (EDQM); (3) Liaise with regulatory agencies including EMA and FDA; and (4) Develop new SOPs for nonclinical and clinical development in close collaboration with ATMP developers. T18.1. aligns with GO:2; SO:1,2,4,5; OO:2-5. T18.2. Regulatory support to clinical research (M1-M84) TL: FGB, AZ*; Contributors: TEDDY. Task 18.2. will provide advice on regulatory requirements with clinical research and regulatory procedures. This support will encompass different types of clinical studies and regulatory procedures. The research specificities will be addressed: paediatric provisions across all paediatric age groups in case of paediatric studies, provisions for genetic, clinical studies with ATMPs according to Reg. 1394/2007/EC. The Regulatory support group will provide beneficiaries with sources, guidance, recommendations, and webinars on the use of data and samples collected during both routine care and clinical studies for regulatory purposes, e.g. dossiers for marketing authorisation applications of medicines and medical devices, clinical studies. Other aspects will be addressed based on the beneficiaries needs. The Regulatory support group will work with the EAB, the Data hub, the Consultancy service, the CRNs, and the Accelerator Hub. It will facilitate engagement with regulatory agencies, including the EMA, to receive the proper support/advice. The group will also help to identify the most suitable regulatory procedures where the research activities need to be included. Whenever relevant, other regulatory agencies/authorities will be addressed as well. T18.2. aligns with GO:2; SO:1,2,4,5; OO:2-5.

Work package WP19 – Methodological support

Work Package Number	WP19	Lead Beneficiary	24 - APHP
Work Package Name	Methodological support		
Start Month	1	End Month	84

Objectives
To contribute to the knowledge transfer of (bio)statistical, data scientific, epidemiological, AI, and ML expertise with the CRNs and other partners. The emphasis is on CTs, epidemiological studies, registries, RWD, and combinations thereof. This rests on state-of-the art methodology and its implementation. When the clinical trial topics have been consolidated, methodology will be further refined and updated. We will contribute to the WP17 Mentoring and Consultancy within the broad competence of the participating partners. A strong interaction will be foreseen with the WP Data Readiness, the WP Real World Data, the WP Finding and Accessing the Data Ecosystem, the WP Data Readiness Services, and the WP Data Sharing and Analysis Services.

Description
T19.1. Methodological knowledge transfer towards local clinical trial teams (M1-M84) TL: APHP, INSERM_U1138,

SFU; Contributors: UHASSELT, UKA. Innovative CT designs tailored to small sample sizes are needed for RDs. Often, CT units in the field do not dispose of adequate knowledge or experts to plan CTs using designs for RDs (tailored to patient's heterogeneity, small sample setting, non-standard endpoints, etc.). We will transfer knowledge in terms of (1) proposing suitable designs for RD clinical questions, (2) providing help in the protocol writing, (3) discussing computational code or statistical package, (4) providing support during the conduct of the trial and in the trial analysis, and (5) participating to the scientific manuscript writing. The idea is not to replace the work of the local teams but to transfer the expert's knowledge, tools, and confidence as a learning process. Local team should be able to use the first trial as an opportunity to develop new skills to be used in future studies. T19.1. aligns with GO:2; SO:1,2,4,5; OO:2,3.
T19.2. Novel methodology for the use of all available knowledge, including RWD (M1-M84) TL: INSERM_1138, UHASSELT, APHP; Contributors: PLUS. T19.2. aims to better characterise and understand patient's disease trajectories and treatments, in RD, one uses multiple data source coming from patients (i.e., real-world data, registries, clinical trial data, patient reported outcomes, etc.) and preclinical trials findings on the disease pathway and mechanism. Incorporating this knowledge into the design of a clinical trial or RWE is not straightforward and it requires specific methodological considerations. We will propose statistical and ML approaches to maximize the use of existing knowledge. We will propose multi-modal approaches, allowing modelling and analysing multisource (preclinical and clinical) and multidimensional (omics, etc.) data. This will benefit clinical trialists and,
evidently patients, as the methodology will enrich information available from trials and therefore enable reducing their length and size. T19.2. aligns with GO:2; SO:1,2,4,5; OO:2-5.
T19.3. Data analysis methodology when data are multivariate, hierarchical, incomplete, and of differing data types (M1-M84) TL: UHASSELT, PLUS, APHP; Contributors: UU. In CTs, real-world studies, and other supporting data, data structures are complex (e.g., data of different outcome types, longitudinally collected), yet using the full complexity increases the chances of successful, shorter, and cheaper trials. Adequate models are needed. Their computational feasibility needs to be ascertained, in view of small sample sizes. The use of surrogate marker methodology will further enhance the methodology. Whereas in common diseases it allows to reduce sample size, in the RD context, it can ensure that the maximally available sample size provides enough information to test a clinically meaningful hypothesis. When data are incomplete, the primary analysis strategy should be chosen so that the assumption of Missingness at Random applies. Then, sensitivity analyses should be done to investigate the stability of the results. This has set in motion an entirely new strand of currently ongoing research, ranging from new modelling strategies for incomplete data (e.g., based on multiple imputation), over sensitivity analysis, to computational strategies. This will improve the design and conduct of CTs in RD. T19.3. aligns with GO:1,2; SO:1,4,5; OO:2-5.
T19.4. Non-parametric, pharmacometrics and randomization-based methodology (M1-M84) TL: UKA, UU, APHP; Contributors: PLUS, UHASSELT. Methods such as generalized pairwise comparisons have been developed for multiple outcomes, either when a hierarchy in the outcomes is present, or when this is not the case. Their place in the context of RDs should be carefully considered. On the one hand, they are computationally convenient, on the other, their power properties need to be examined for a given trial, such as considered within a CRN. Simulation based evaluation, tailored to the needs of a specific research question, in the context of a specific RD, should be undertaken. Pharmacometrics models based on nonlinear mixed effects analysis of longitudinal data are particularly suitable for RD, given their ability of making use of all relevant data in a structure that allows the use of prior
information. T19.4. aligns with GO:2; SO:1,2,4,5; OO:2,3.

Work package WP20 – Education and Training on RD Research

Work Package Number	WP20	**Lead Beneficiary**	26 - EURORDIS
Work Package Name	Education and Training on RD Research		
Start Month	1	**End Month**	84

Objectives
To develop a comprehensive programme of education and training on RD research serving the needs across career stages, the R&I pipeline and multistakeholder communities. Specific objectives: (1) Empower patient representatives to enable their full-scale involvement into RD research (T20.1); (2) Support the RD-focused career development of young researchers (T20.1 and T20.4); (3) Empower the RD community for participation in ERDERA and beyond (T20.2 and T20.3); (4) Enable wide dissemination of education and training into national systems (T20.2 and T20.3); and (5) Enable continuous identification and fulfilment of novel, arising cutting-edge education and training needs in tight interaction with all ERDERA workstreams (T20.2.).

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Description
T20.1. Patients and young researchers' trainings (M1-M84) TL: EURORDIS; Contributors: WDO, DDF, GA UK*, c4c-S, TEDDY, IMAGINE, LUMC. T20.1. aims to train patients and young researchers about the fundamentals of RD research. Training topics will be aligned with ERDERA needs and work streams, specifically the CRNs as they constitute a new component of the RD ecosystem. The core part will rely on the existing EURORDIS Open Academy and will be a scalable approach of training patients and young researchers through a 3-step programme: i) beginner level, ii) intermediate level, iii) advanced level. A strong emphasis will be put on mutual learning from patients and researchers. The training will be delivered through a blended, dynamic, and interactive approach, considering the learning specificities of each target audience. 2-3000 people a year (30% outside of EU) will be trained through the beginner level; up to 100 through the intermediate level (specialised pathways, face-to-face) and at least 30 through the advanced level (online, "Master Classes"). Patient experts participating in ERDERA calls' evaluation (WP3-4-5) would have completed at least the first two levels. An annual workshop will also be organized for up to 20 young patients (12-18 years old) building upon EJP RD paediatric trainings. T20.1. aligns with GO:3; SO:3,4; OO:1,3,4. T20.2. Identification and fulfilment of training needs (M1-M84) TL: VULSK, ASU FC; Contributors: EURORDIS, FFRD, UCSC. T20.2. aims to ensure a continuous process for identification of education and training needs and to create a strong basis for the introduction of new trainings. T20.2. aligns with GO:3; SO:4; OO:2,3,4. ST20.2.1 Continuous identification of training needs (M1-M84) will be performed using different sources: ERDERA workstreams; NMGs (with WP23); interaction with the global RD ecosystem (with WP25). ST20.2.2 Implementation of novel horizon-scanning trainings (M13-M84). For novel arising needs, expert-level horizon-scanning trainings will be organized with the engagement of the most prominent experts in the field. ST20.2.3. Implementation of the train-the-trainer principle (M1-M84). National training needs will be identified and implemented in collaboration with WP23 applying the train-the-trainer principle to achieve a "snowball effect": inclusion and dedicated support for national representatives in WP20 and implementation of adapted national trainings in WP23. Providers of education and training will define standardization rules for national training programmes and will support and supervise national trainers. At year 3, evaluation of the state-of-the-art of the ERDERA research and education programme will be accomplished to inform further developments. T20.3. RD research trainings for multistakeholder communities (M1-M84) TL: CNAG, VULSK; Contributors: UT, SRUMC, UTARTU, TUM, EATRIS, GA UK*, Fraunhofer UK*, ECRIN, SFU, UHASSELT, ISS, LUMC, UMCG, AUMC, WDO, DDF, UTWENTE. T20.3. aims to equip the RD-research-related multistakeholder community with the knowledge and skills needed for effective participation in ERDERA activities and beyond. Five subtasks are arranged to reflect targeted training blocks benefiting the main ERDERA Work streams to empower: (1) RD diagnostic research; (2) RD clinical research; (3) knowledge on research methodologies; (4) RD clinical trial methodologies and management; and (5) data research. A graded scalable approach will be implemented: beginner-level (mostly online trainings), followed by advanced-level, and/or nationally adapted online or face-to-face trainings for selected highly motivated learners who accomplished the beginner-level trainings and reached a certain level of expertise. Up to several hundreds of trainees per year will benefit from each beginner-level training and 20-30 selected trainees will be trained on an advanced course (for each of the 5 training tracks). The most effective training methodologies will be applied and measures for broad dissemination and inclusion will be invoked (incl. rotation of courses and fellowships for participants from underrepresented countries). T20.3. aligns with GO:1,2,3; SO:2,3,4,5; OO:2,3,4. T20.4. European Diploma on RD research (M1-M84) TL: UCSC, IBG; Contributors: c4c-S, ISS, SU, UNIROMA1, ISCIII, ACU, UCD, RSU, VULSK, SFU. T20.4. aims to establish a higher education program culminating in an academic diploma with credits, through an inter-university consortium of academic and non-academic partners with track record in RD training activities. T20.4. aligns with GO:1; SO:4,5; OO:3,4. ST20.4.1. Establish a cross ERDERA expert consortium and setup of training modules (M1-M12). Multilateral agreements will be made among academic and non-academic partners and connections with European university alliances, to ensure policy alignment and improve geographical representation as well as to ensure the smooth integration of young RD researchers into the EU R&I ecosystem. ST20.4.2. Pilot program launch (M13-24). This will run as a short-time pilot program (min 10 ECTS). ST20.4.3. Optimization and scale-up of the program (M25-36). The study plan will be refined and potentially upgraded to longer-term education programs to address emerging needs and provide recognized diplomas. ST20.4.4. Running the first systematic EU diploma curriculum (M30-60). Enrolling the first cohort of students, the curriculum will include a transnational mobility schedule and teaching modules from different partners. ST20.4.5. Optimization and updating of study plan (M52-M84). Continuing adaptation of the course. ST20.4.6. Pursue future sustainability of the established curricula (M6-84). Collaboration with stakeholders will be established to secure the program's sustainability (incl. opportunities offered through Erasmus Mundus programme).

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Work package WP21 – Technology accelerator

Work Package Number	WP21	Lead Beneficiary	28 - UC
Work Package Name	Technology accelerator		
Start Month	1	End Month	60

Objectives

To increase the success of in vivo ATMP therapies by improving state of the art technologies, processes, standards, and tools that are critical for efficacious and safe in vivo ATMPs. An open access portfolio of solutions and a network of expertise will be created in Europe which will decrease the number of therapies that fail in development and contribute to SO5, delivering new effective therapies for rare diseases approved in the EU and beyond (GO2). This will be achieved through cost-effective and harmonized AAV gene therapy; advancing RNAs for therapeutics; novel types of RNA nanoparticles (NP); comparative evaluation of gene editing technologies and delivery in relevant model systems for RDs; and development of platforms to characterize therapy response.

Description

T21.1. Streamlining chemistry manufacturing and controls in AAV vector production (M1-M60) TL: KU Leuven, UCB*, GNT. Contributors: VHIR, UC, UAB, INSERM_Target(Nantes), FHG, PEI, UKHD, REI*, Miltenyi*, FDB*, ROCHE*. Cost-effective and harmonized rAAV gene therapy vector development will be enabled through the development of a publicly available base manufacturing process to support next generation rAAV development and validation of new methodologies to ensure high quality and safety of newly
standardized vectors. Fit-for-purpose analytical assays for determining CQA-related rAAV characteristics will be defined and validated. New technologies to develop more accurate analytical methods will be developed. T21.1. aligns with GO:2; SO:1,4,5; OO:1,2,5.
T21.2. Advancing RNAs for therapeutics (M1-M60) TL: UC, Pfizer*, FHG. Contributors: INSERM_ART-ARNm, CHARITE, UEF, PEI, FSJD-CERCA, GNT, RJF*, AZ*, Miltenyi*, HIPRA*, LAB HIPRA*, FDB*. Approaches for RNA manufacturing will be optimized to advance the state of the art for mRNA therapeutics and ensure higher stability, translatability, cell-specificity, and lower immunogenicity. This will involve improving RNA design, production and purification, analytical characterization, and screening of optimal RNA molecules. A head-to-head comparison of RNA sequences will be conducted in in reporter cell lines to assess and compare the efficacy of selected RNA sequences (e.g., delivery of gene editing tools for stable gene therapy and gene replacement). Selected RNAs will be used in subtasks T21.3 and T21.4. T21.2. aligns with GO:2; SO:1,4,5; OO:1,2,5.
T21.3. Advancing of novel types of mRNA nanoparticles (NP) including LNP, extracellular vesicles (EVs) and biohybrids (M1-M60) TL: INSERM_ART-ARNm, Pfizer*, CNRS. Contributors: FHG, PEI, UC, CHARITE, CIBER, VHIR, PLUS, UEF, Miltenyi*, AZ*, RJF*, HIPRA*, LAB HIPRA*, FDB*, ROCHE*. A better mechanistic understanding of extra and intracellular barriers to mRNA delivery via NP/EVs will allow a more rational design of novel mRNA formulations, including targeting tissue types along with improved and sustained
release. In accordance, tools to implement formulation design, efficiency, production of standardized protocols will be developed. Different mRNA formulations will be generated with optimal mRNA structures produced in T21.2 and will be scaled-up for use for RNA-based gene editing, and evaluation of therapy response. T21.3. aligns with GO:2; SO:1,4; OO:1,2.
T21.4. Gene editing approaches towards therapy of RDs (M1-M60) TL: OSR, Miltenyi*, IMAGINE. Contributors: UC, CIBER, GNT, UKLFR, BIU, UAB, FSJD-CERCA, FTELE, AZ*, Pfizer*, FDB*, ROCHE*. Comparison of state-of-the-art gene editing technologies and capitalize on viral and non-viral gene delivery modalities optimized in T21.1-3 to develop novel, more effective and safer therapeutic approaches for paradigmatic RDs affecting the blood, the central nervous system, the striated muscle, the retina, and the liver. We will complement these in vitro and in vivo gene therapy studies with an in-dept characterization of editing specificity and treatment-related toxicities, including immune responses and strategies to avoid them (T21.5), thus providing robust pre-clinical packages exploitable for the nomination of diseases suitable for clinical development. T21.4. aligns with GO:2; SO:1; OO:1.
T21.5. Assessment of therapy response and immunogenicity (M1-M60) TL: CHARITE, Pfizer*; Contributors: CHI, Miltenyi*, ROCHE*, FSJD-CERCA, UAB, UC, OSR, INSERM_Target(Nantes), AZ*, UCB*. T21.5. aims to develop, qualify, and validate complex platforms used to characterize and monitor immune reactions directed to the developed ATMP. In vivo and in vitro tissue model systems will be used to verify the feasibility of test platforms developed. Mitigation strategies to prevent/overcome unwanted immune response will be developed. T21.5. aligns with GO:2; SO:1,4; OO:1,2.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Work package WP22 – Public-Private Collaboration accelerator

Work Package Number	WP22	Lead Beneficiary	29 - FFRD
Work Package Name	Public-Private Collaboration accelerator		
Start Month	1	End Month	84

Objectives
To create and operate an innovation marketplace, supporting and connecting promising RD projects with R&D experts, patient groups, and public and private investors, to enable further development. WP22 is dedicated to GO2, SO1. Specifically: (1) Engage third party investors, pharma industry and other funders of innovation; (2) Create workflows and legal documentation necessary to structurally identify, evaluate and select projects; (3) Support selected projects to become investment ready through business planning, coaching, nonclinical development, also in collaboration with other relevant synergistic initiatives; and (5) Actively match projects to external investment opportunities.

Description
T22.1. Setting up the marketplace (M1-M12) TL: ISCIII; Contributors: AFM, EATRIS, FFRD, SRUMC, EURORDIS. ISCIII will define the process workflows and create the legal documentation (working with RUMC and EATRIS) to facilitate sharing of information in the accelerator. Of particular importance are confidentiality and conflict of interest declarations, also with external collaborators. Experts from Expertise Service Hub, as well as external experts, e.g. from REMEDi4ALL, C-Path and C4C will be utilized as needed. FFRD will liaise with prospective investors and onboard them (using letters of intent to express interest) into the marketplace. AFM (with input from FFRD and EURORDIS) will define the project selection process, connecting with WP17 mentoring and consultancy creating workflows to be able to utilize their expertise, WP4 CRN and WP3 JTC to set up the outreach and project identification process within JTCs and the CRNs. T22.1. aligns with GO:2; SO:4,5; OO:3,5. T22.2. Acceleration readiness (M1-M72) TL: AFM; Contributors: EATRIS, FFRD, EURORDIS. During JTC calls, information sessions will be integrated in the call publication strategy, as well as monitoring process of JTC projects to ensure all applicants and Principal investigators are fully aware of the requirements for further therapeutic development and the opportunities provided by the Acceleration Hub, Expertise Hub, and infrastructures. Annual meetings will be organized in liaison with JTC and monitoring WPs to identify JTC projects with potential for development into new intervention. Identified projects will then be proposed to enter profiling and development process in the Acceleration Hub (T22.3). Close collaboration with all WP22 partners will be sought for the selection of projects, with structural involvement of patient representatives in the selection process. During JTC calls: integrate information sessions in the monitoring process of JTC projects (and projects from ERA4HEALTH) to ensure investigators are fully aware of the requirements for further development and the opportunities provided by the Acceleration Hub, Expertise Hub, and infrastructures. T22.2. aligns with GO:2; SO:1,4; OO:1,3,5. T22.3. Asset profiling and development (M12-M80) TL: EATRIS; Contributors: AFM, FFRD, EURORDIS, ISCIII. Selected projects will receive support defining an IPR, exploitation and patient access strategy, designing a critical path to proof of concept including stage gates and milestones, seeking funding for technical development. Expertise from CRNs, Consulting and Mentoring WPs will be accessed, as well as other initiatives such as C-Path, C4C, REMEDi4ALL, EU Lead Factory. It is expected that 5-10 projects per year can be supported, with first projects receiving support from M18. T22.3. aligns with GO:2; SO:1,4; OO:1,3, 5. T22.4. Matchmaking and marketing (M18-M84) TL: FFRD; Contributors: AFM, EATRIS. Regular interactions with pharma and other potential funders will be scheduled to pitch projects and facilitate discussions and negotiations. A range of different formats will be used including webinars of pitches (presentations + Q/A sessions), networking events, speed dating events between researchers and funders, and set-up of F2F meetings to discuss potential collaboration. Coaching of researchers, creation of pitch decks and support in pitching to third party funders, based on the creation of a grid including key elements such as identified and validated target, PI, mechanism of action and competitive landscape analysis. Marketing of the accelerator program and the projects in the portfolio will be conducted on an ongoing basis, with direct outreach to investors. T22.4. aligns with GO:2; SO:1, 4,5; OO:1,3,5.

Work package WP23 – NMGs promotion and national alignment

Work Package Number	WP23	Lead Beneficiary	1 - INSERM

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Work Package Name	NMGs promotion and national alignment		
Start Month	1	End Month	84

Objectives

The main objective of this WP is to ensure the alignment of European and national RD research policies and activities by supporting the deployment, the operations, and the synergies of and between the National Mirror Groups (NMGs) in all participating countries. An NMG is a group created – or designated - in each country, benefiting from the ERDERA to bring together the expertise and knowledge of the RD community of a specific country. The objectives of a NMG are to identify national needs that should be discussed and addressed, if possible, within the framework of the ERDERA activities; to coordinate national stakeholders and promote national alignment with the European RD research strategy, to revitalize the national RD plans/strategies and to collect and share lessons learned and good practices. NMGs will also be solicited to help with liaising with the national stakeholders, including but not limited to funders, to manage the lessons learned from the cancer field and organise, when relevant, joint activities (like common or complementary funding opportunities).

Description

T23.1. Fostering creation of NMGs (M1-M84) TL: INSERM_IT-GGB; Contributors: ISCIII, UNEW*, CCRI GmbH, UTARTU, IBG, CCUH, INSERM_U974, MUH, TIF, MICYRN*, VULSK, ZonMw, INSA, HRB, MoH SR, RDG, JSI, UO. T23.1. aligns with GO:1-3, SO:5, OO:3 and will consist of two subtasks.
ST23.1.1. Development of NMG models and guidelines. In the first 4 months of the project, several models of NMGs will be developed based on the study of the national groups created during EJP RD. These different models, which will differ in several aspects, will be used on the NMGs development process on the Task 23.1.2.
ST23.1.2. Developing & maintaining NMGs through a national multi-stakeholder engagement. The NMGs will be set up and supported to organize coordinated interaction between the ERDERA and national and regional stakeholders. To provide successful action of NMG, financial support will be provided to each NMG.
T23.2. Deployment and operation of NMGs (M1-M84) TL: UNEW*; Contributor: INSERM_IT-GGB, ISCIII, CCRI GmbH, UTARTU, IBG, CCUH, INSERM_U974, MUH, TIF, MICYRN*, VULSK, ZonMw, INSA, HRB, MoH SR, RDG, JSI, UO. T23.2. aligns with GO:1-3; SO:4,5; OO:3,4 and will consist of four subtasks.
ST23.2.1. NMG responsibilities. Each NMG should fulfil their responsibilities to ensure optimal collaboration with ERDERA. Fulfilling responsibilities will help advocate national interests and provide bidirectional information flow from and to partnership. During the first 3 years of the project, WP leads will support the deployment and operation of new and existing NMGs. This will include supporting NMGs to develop a three-year plan for their NMG. In the following four years of the project, NMG leads will continue to maintain and
develop their NMG with support from WP leads.
ST23.2.2. Country-Specific multidirectional Engagement. The WP leads will ensure regular communication with NMG teams to support them in aligning their national activities with those delivered under the ERDERA. During the first three years of the project, communication channels will be established WP leads and NMGs, as well between NMGs to support multi-directional engagement. WP leads will work with other WPs to communicate the sharing of tools, resources and knowledge developed by other WP to the NMGS.
ST23.2.3. Country Data Collection. A number (minimum one per year) of questionnaires will be designed to collect RD data on national activities and international collaborations. Outputs will be dedicated to annual reports and guideline development. This will continue throughout the project.
ST23.2.4. Trainings activities through the ‘Train the trainer model’. A series of training activities for national stakeholders is planned. This subtask will collaborate with ERDERA Workstream ‘Education & training activities. Each NMG will identify a national training provider and will be trained on the topic preselected by NMGs. Once trained, they will then be able to share what they have learned at national level to national stakeholders.
T23.3. Animation of NMGs synergies (M6-M84) TL: UNEW*, CCUH; Contributors: INSERM_IT-GGB, UTARTU, CCRI GmbH, ISCIII, VULSK, ZonMw, INSA, MICYRN*, INSERM_U974, MUH, TIF, IBG, HRB, MoH SR, RDG, JSI, UO. T23.3. aligns with GO:1-3; SO:5; OO:3,5 and will consist of three subtasks.
ST23.3.1. Organization of annual meeting of the National Alignment Board (NAB), foreseen back-to-back with the annual General Assembly. NAB will be composed of Representatives from each NMG and Representatives of the EC Directorates. During these meetings, NMG leads will share progress on the creation and operations of NMGs, and steps taken to align national and ERDERA level activity. These meetings will also serve as a basis for writing of best practice guidelines on NMG creation and promotion in first three years of partnership. During the next four years, the recommendations for sustainability of NMGs will be developed.
ST23.3.2. Fostering interaction between NMGs, to enhance cross-country collaboration. Three workshops will be

organized during first three years, followed by four in the last four years, topics of which will be identified during International NAB meeting, but foreseeably include subjects such as creation/adaptation/federation of national registries for RD, linking national diagnostics structures with ERDERA resources, optimising clinical trial planning and delivery, national drug reimbursement programs, NBS etc. During this subtask intensive collaboration and communication in between various sets of NMGs on monthly or even weekly basis will be coordinated and facilitated using some platform for example SharePoint.
ST23.3.3. Sharing achievements of NMGs. During the first three years of partnership using the outputs of T23.2.3, an overview report will be developed every year, arranged by topic (e.g. showcasing the situation and trends around live national plans for RD, national registries for RD, etc). During the following four years four more reports will be developed and two peer-reviewed publications in open access journals will be published during project with a purpose to reach out more health care specialists, for example GPs, clinical specialists, and scientists from other fields.

Work package WP24 – Fostering engagement of underrepresented countries in ERDERA

Work Package Number	WP24	**Lead Beneficiary**	32 - AICIB
Work Package Name	Fostering engagement of underrepresented countries in ERDERA		
Start Month	1	**End Month**	84

Objectives

(1) Address specific needs and expectations of underrepresented countries (UCs) in RD; (2) Foster collaboration between UCs and Research & Innovation (R&I) high performing countries at European and Global level; (3) Boost inclusion of UCs in ERDERA funded programmes; (4) Promote transversal, coordinated efforts in mapping capabilities and assets, capacity development, advocacy, awareness-raising, and leveraging the knowledge and experiences of UCs with R&I high performing countries; (5) Create a more inclusive and impactful R&I ecosystem in RD; and (6) De-emphasize the inequalities between R&I high and low performing countries and unlock the potential present within UCs and its added value to the ERDERA.

Description

T24.1. Promoting capacity development actions (M1-M84) TL: VULSK, REUH; Contributors: EURORDIS, IBG, CVBF, GERAD, UCD. T24.1. aims to (1) Develop a mapping exercise to identify specific needs and expectations, perceived by UCs as limiting their full integration in RD R&I, aligned with ERDERA workstreams; (2) Assess the conditions for their full integration across all ERDERA activities (JTCs, CRNs, Acceleration Hub, Data Services Hub, Support Services), including potential barriers to participation in CTs; (3) Implement knowledge exchange and mutual learning exercises between UCs (research actors, patient organisations) for comparative assessment and promotion of activities, at National level, to foster participation in ERDERA. Complementation of efforts for the coordination of the National Mirror Group representatives; (4) Benchmark high performing countries in R&I to integrate learnings and expertise; and (5) Develop focused guidelines for potential actions at the National level (e.g., national calls to support specific lines of research aligned with CRNs objectives). T24.1. aligns with GO:3, SO:4-5.
T24.2. Undertaking advocacy and awareness efforts to UCs added value (M1-M84) TL: FFRD, IBG, CAU; Contributors: EURORDIS, RSU, RDB. T24.2. aims to (1) Detect latent and unknown RDrelated assets in UCs countries, and additional patient populations, to convert it into added value for the ERDERA; (2) Implement measures to identify RDs with particular (geographic) incidence, distinctive critical mass, and infrastructural resources; (3) Establish synergies with JARDIN, EURORDIS, HNN3.0 (Health NCPs), NFP4EU (Health NFPs), and NCP_WIDERA.NET, to get further support for the identification of UCs added value; (4) Collaborate with national entities, National Mirror Groups and scientific societies for the assessment of distinctive features of UCs; (5) Pursuance of advocacy and awareness actions (to be undertaken with the coordination of ERDERA and of the workstreams) to promote their inclusion in the ERDERA activities; and (6) Alignment of academic, clinical, and patient organisations, at the national level, and promotion of the geographical regions (North Africa, Eastern Europe, and Southern Europe countries). T24.2. aligns with GO:3; SO:3,5; OO:3.
T24.3. Support actions to improve UC participation in all ERDERA activities (M1-M84) TL: AICIB, IMGGE; Contributors: TUBITAK, RIF, ZonMw, VULSK, EURORDIS, CVBF, HRB. T24.3. aims to (1) Identify actions to increase the participation of UCs RD community in ERDERA, and of the funds available for both UCs and ERDERA partners; (2) Develop guidelines for promoting the inclusion of UCs in ERDERA funded actions (e.g., JTCs, Networking Calls, and others) in coordination with the WS Leads; (3) Propose new measures to increase UCs participation using

the outputs of the mapping of needs, lessons learnt from EJPRD, EURORDIS surveys, and other relevant initiatives; (4) Establish baseline figures, and proposal of targets for levels of participation in these activities; (5) Analysis and adaptation of measures and guidelines used in the Widening programmes (e.g., Twinning, Excellence Hubs, Hop-on), and their application to ERDERA activities (when appropriate); and (5) Exploitation of access to additional financial support (e.g. EU Widening programmes, structural funds) to increase UCs participation in ERDERA and leverage available funds, and propose measures to be implemented (also to be highlighted to the National Mirror Groups). T24.3. aligns with GO:3; SO:5.

Work package WP25 – ERDERA Global Collaborations

Work Package Number	WP25	**Lead Beneficiary**	7 - ZonMw
Work Package Name	ERDERA Global Collaborations		
Start Month	1	**End Month**	84

Objectives

To establish international partnerships that will benefit ERDERA and promote sharing of resources, expertise, and research findings which will address issues of resource fragmentation, harness collective knowledge and expertise, and facilitate exchange of information and data, ultimately leading to improved diagnosis and the development of new and innovative treatments for RDs.

Description

T25.1. Strategic Alliances (M1-M84) TL: INSERM_IT-GGB, SU, ZonMw; Contributors: RCC*, CIHR*, RDI, EURORDIS, FFRD, ISCIII, AICIB, CAU, AUMC, ASU-FC, HSJD. In collaboration with WP1 and other ERDERA WPs, T25.1. aims to foster effective international collaboration and maximize outreach of the results of ERDERA through strategic alliances. T25.1. will be subdivided in four subtasks. INSERM_IT-GGB and Sorbonne University will start in parallel the mapping of potential international strategic alliances encompassing universities, programs, projects (including EJP RD and ERDERA funded projects), and initiatives that have not yet been identified in the SRIA/EJP RD/ concept Partnership. Recommendations from IRDiRC members will be sought to augment this process. Following this initial mapping, a dedicated Working Group composed of contributors, and ERDERA partners will further develop the collated list of identified international strategic partners and will facilitate partner matchmaking by identifying the specific topics and opportunities for collaboration across different ERDERA WPs. Throughout the duration of ERDERA, regular virtual meetings will be organised to discuss progress, share updates and outcomes, and address any challenges or opportunities that may arise during the existence of ERDERA. The identification of additional strategic partners and opportunities will be continuously performed and in collaboration with WP1, a sustainability plan of the established partnerships will be developed. T25.1. aligns with GO:1-3; SO:4,5; OO:2,3,5.

T25.2 Support to IRDiRC Scientific Secretariat (M1-M84) TL: FFRD; Contributors: TEAMIT. FFRD will secure the IRDiRC Scientific Secretariat (SciSec), which plays a vital role in the day-to-day operations and management of the IRDiRC Consortium. As key administrative and scientific support unit, SciSec ensures the fulfilment of IRDiRC's needs and requests, assisting various bodies such as the Consortium Assembly, Constituent Committees, Scientific Committees, Operating Committee, Task Forces, and Working Groups, optimizing their complementary activities. SciSec will continue to organize and coordinate Consortium Assembly in-person and online meetings, including joint meetings with Scientific Committees, Task Force workshops, and IRDiRC Congress. SciSec will coordinate the Consortium's communication activities and delivers comprehensive meeting reports that capture the outcomes and discussions of these events and activities, including participation in the writing of white paper/recommendations of IRDiRC Task Forces. To ensure liaison between ERDERA and IRDiRC stakeholders, SciSec members will present IRDiRC updates to ERDERA Executive Committee and organize dedicated IRDiRC sessions during ERDERA General Assembly meetings. In addition, ERDERA beneficiaries' involvement in IRDiRC activities will be promoted, and the IRDiRC Chair and Vice-Chair will be invited to join the ERDERA MAB. T25.2. aligns with GO:1-3; SO:4-5; OO:3,5.

T25.3. Promote the International Dimension of the CRN of ERDERA by building global networks among CRNs and patient organizations (M1-M84) TL: RDI, INSERM_IT-GGB; Contributors: AICIB, AUMC, c4c-S, UKHD, UT, CHEO-RI*, RCC*. T25.3. aims to perform networking, matchmaking, and identifying similar initiatives as the CRNs, that exist in other geographies. In collaboration with the Workstream on CRN, international CRN conferences will be organised to facilitate networking between various international CRNs, jointly organized with IRDiRC, RDI, and ERDERA. The

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conferences will be organised on biannual basis and may be organised in conjunction with the IRDiRC-ERDERA Congress. T25.3. aligns with GO:2,3; SO:3-5; OO:2,3,5.
T25.4 Alignment with the Research strategies of the European Reference Networks (M1-M84) TL: ASU-FC, HSJD; Contributor: IOR. T25.4 aims to align research strategies within the ERNs and with ERDERA. A platform "ERNs Living Lab" will be created to foster new cross-fertilising communication and avenues across ERNs and stakeholders to accelerate patient-relevant advancements and discuss the alignment of research strategies and implementation of the acquired knowledge in activities of ERDERA and beyond. T25.4. aligns with GO:3;
SO:1,4,5; OO:3-5.

Work package WP26 – Ethics requirements

Work Package Number	WP26	**Lead Beneficiary**	1 - INSERM
Work Package Name	Ethics requirements		
Start Month	1	**End Month**	84

Objectives
The objective is to ensure compliance with the 'ethics requirements' set out in this work package.

Description
This work package sets out the 'ethics requirements' that the project must comply with.

STAFF EFFORT

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	WP10	Total Person-Months
1 - INSERM	288.00					125.00	12.00		6.00		828.00
1.1 - CAD						6.00	22.00				72.00
2 - TEAMIT	36.00	72.00									126.00
3 - DLR	3.00		20.00	8.00							31.00
4 - ANR	3.00		19.00		1.00						23.00
5 - FTELE			2.00	17.00							66.00
6 - LMT			2.00		4.00						6.00
7 - ZonMw	3.00		6.00		10.00						44.00
8 - UT						78.00	66.00	33.00	57.00	30.00	300.00
9 - UTARTU						42.00					56.00
10 - CNAG						72.00	105.00	6.00			278.00
11 - SRUMC						6.00	153.00	121.00	34.00		356.00
12 - TUM						6.00		76.00			84.00
13 - UKHD									152.00	76.00	279.00
14 - C-PATH									80.00		107.00
15 - VHIR									27.00	76.00	134.00
16 - LUMC						6.00			27.00		118.00
17 - UTWENTE											38.00
18 - UPM									27.00	28.00	149.00

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	WP10	Total Person-Months
19 - UMCG						29.00		15.00			166.00
20 - AUMC	3.00										67.00
21 - UM											36.00
22 - EATRIS											86.00
23 - FGB	36.00				2.00						93.00
24 - APHP						6.00			89.00	42.00	169.00
25 - UHASSELT											35.00
26 - EURORDIS	12.00		3.00		1.00					8.00	124.00
27 - VULSK	3.00					6.00		18.00			100.00
28 - UC											57.00
29 - FFRD			5.00		2.00						146.00
30 - AFM	8.00										44.00
31 - CCUH											30.00
32 - AICIB	3.00										23.00
33 - IMGGE											15.00
34 - RDI	5.00									2.00	19.00
35 - ACU											2.00
36 - AIT											23.00
37 - AMU								12.00			26.00
38 - AOU Meyer IRCCS						9.00					9.00
39 - ASU-FC											35.00

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	WP10	Total Person-Months
40 - BIU											3.00
42 - CCRI GmbH						6.00		18.00			36.00
43 - CENTOGENE						7.00	11.00				18.00
44 - CHARITE											61.00
45 - CHI											20.00
46 - CHU Dijon						9.00	18.00				27.00
47 - CE	54.00										54.00
48 - REGIONH						6.00		12.00			18.00
49 - CSO-MOH	18.00		2.00		1.00						21.00
50 - CVBF	18.00									2.00	31.00
51 - DDF									26.00		44.00
53 - Erasmus MC						9.00			15.00	44.00	68.00
54 - F.R.S.-FNRS			2.00								2.00
55 - FHG											62.00
56 - FRRB			2.00								2.00
57 - ECRIN											5.00
58 - FWF			2.00								2.00
59 - IFD			2.00								2.00
60 - FSJD-CERCA											23.00
61 - FCT			2.00								2.00
62.1 - AZV			2.00								2.00

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	WP10	Total Person-Months
63 - GNT											102.00
64 - GERAD											5.00
65 - RS						3.00	1.00				4.00
66 - GUF											11.00
67 - HRB			2.00								18.00
68 - İBG						6.00	7.00	6.00			56.00
69 - Rannis			2.00								2.00
70 - IMAGINE							12.00				49.00
71 - IGC PAN						6.00					6.00
72 - ISCIII			17.00				36.00				76.00
73 - INSA											12.00
74 - IOR											3.00
75 - ISS											11.00
76 - IT-MOH			2.00								2.00
77 - KU Leuven						6.00	10.00				53.00
78 - LZP			2.00								2.00
79 - MRT											27.00
80 - MUS						6.00					6.00
81 - MUH						6.00		18.00			36.00
82 - MUR			2.00								2.00
83 - NCBR			2.00								2.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	WP10	Total Person-Months
84 - NKUA						6.00					6.00
85 - MoH SR											12.00
86 - RDG											8.00
87 - REGIONSYD						18.00					18.00
88 - OPBG						9.00		12.00			21.00
89 - OSR											43.00
90 - JSI											8.00
91 - RCN			2.00								2.00
92 - FWO			2.00								2.00
93 - REUH						9.00					21.00
94 - RIF			2.00								6.00
95 - RCSI						9.00					9.00
96 - RSU											5.00
97 - Sciensano									30.00	18.00	48.00
98 - SPW			2.00								2.00
99 - SFU											26.00
100 - ETAg			2.00								2.00
101 - SAS			2.00								2.00
102 - Sonio											27.00
103 - MOSAE			2.00								2.00
104 - SRC			2.00								2.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	WP10	Total Person-Months
105 - TEDDY											6.00
106 - TEKKARE	66.00										66.00
107 - TIF											12.00
108 - TUBITAK			2.00								6.00
109 - RT (TuscReg)			3.00								3.00
110 - UAB											20.00
111 - UCD											7.00
112 - UCSC											16.00
113 - UEF											27.00
114 - UKA											22.00
115 - UKLFR									30.00		38.00
116 - UNICAMPANIA						9.00					9.00
117 - UoC						6.00					6.00
118 - UGENT						6.00	18.00				24.00
119 - UKCL						9.00					9.00
120 - WDO	5.00		1.00	3.00	1.00					2.00	21.00
121 - UU							18.00				62.00
122 - c4c-S											10.00
123 - CAU											8.00
124 - CNRS											20.00
125 - CIBER						9.00					27.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	WP10	Total Person-Months
126 - UEFISCDI			2.00								2.00
127 - UNIROMA1											9.00
128 - UANTWERPEN						6.00					6.00
129 - BNSF			2.00								2.00
130 - Aalborg UH						6.00					6.00
131 - RDB											3.00
132 - BBMRI-ERIC											8.00
133 - AarhusUH						9.00					9.00
134 - IABS-EU											12.00
135 - HRCI	5.00										5.00
136.1 - KUM									33.00	8.00	41.00
137 - MSW	38.00										38.00
138 - FNR			2.00								2.00
139 - NKFIH			2.00								2.00
140 - PEI											36.00
141 - PLUS											37.00
142 - SU											3.00
143 - UNISI						9.00					9.00
144 - Vinnova			2.00								2.00
145 - CRG-CERCA						15.00					18.00
146 - GMS-RS						3.00	1.00				4.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	WP10	Total Person-Months
147 - VIB						3.00					3.00
148 - IPG						6.00					6.00
149 - UO						6.00					6.00
150 - HSJD											7.00
Total Person-Months	607.00	72.00	132.00	28.00	22.00	614.00	490.00	347.00	633.00	336.00	6355.00

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP11	WP12	WP13	WP14	WP15	WP16	WP17	WP18	WP19	WP20	Total Person-Months
1 - INSERM	84.00		40.00			86.00			23.00		828.00
1.1 - CAD					44.00						72.00
2 - TEAMIT											126.00
3 - DLR											31.00
4 - ANR											23.00
5 - FTELE	36.00										66.00
6 - LMT											6.00
7 - ZonMw											44.00
8 - UT		30.00								6.00	300.00
9 - UTARTU										2.00	56.00
10 - CNAG				5.00	41.00	27.00				22.00	278.00
11 - SRUMC			16.00	15.00						8.00	356.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP11	WP12	WP13	WP14	WP15	WP16	WP17	WP18	WP19	WP20	Total Person-Months
12 - TUM										2.00	84.00
13 - UKHD	18.00	30.00									279.00
14 - C-PATH				27.00							107.00
15 - VHIR							18.00				134.00
16 - LUMC		22.00	31.00	25.00		5.00				2.00	118.00
17 - UTWENTE			26.00	10.00						2.00	38.00
18 - UPM			32.00	37.00	25.00						149.00
19 - UMCG			32.00	10.00	78.00					2.00	166.00
20 - AUMC			18.00	15.00		28.00				2.00	67.00
21 - UM						36.00					36.00
22 - EATRIS							15.00	26.00		9.00	86.00
23 - FGB							5.00	50.00			93.00
24 - APHP									32.00		169.00
25 - UHASSELT									32.00	3.00	35.00
26 - EURORDIS	18.00									64.00	124.00
27 - VULSK										46.00	100.00
28 - UC											57.00
29 - FFRD										6.00	146.00
30 - AFM											44.00
31 - CCUH											30.00
32 - AICIB											23.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP11	WP12	WP13	WP14	WP15	WP16	WP17	WP18	WP19	WP20	Total Person-Months
33 - IMGGE											15.00
34 - RDI											19.00
35 - ACU										2.00	2.00
36 - AIT			16.00	7.00							23.00
37 - AMU						14.00					26.00
38 - AOU Meyer IRCCS											9.00
39 - ASU-FC										25.00	35.00
40 - BIU											3.00
42 - CCRI GmbH											36.00
43 - CENTOGENE											18.00
44 - CHARITE											61.00
45 - CHI											20.00
46 - CHU Dijon											27.00
47 - CE											54.00
48 - REGIONH											18.00
49 - CSO-MOH											21.00
50 - CVBF	6.00										31.00
51 - DDF				12.00						6.00	44.00
53 - Erasmus MC											68.00
54 - F.R.S.-FNRS											2.00
55 - FHG											62.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP11	WP12	WP13	WP14	WP15	WP16	WP17	WP18	WP19	WP20	Total Person-Months
56 - FRRB											2.00
57 - ECRIN										5.00	5.00
58 - FWF											2.00
59 - IFD											2.00
60 - FSJD-CERCA											23.00
61 - FCT											2.00
62.1 - AZV											2.00
63 - GNT	48.00										102.00
64 - GERAD											5.00
65 - RS											4.00
66 - GUF			11.00								11.00
67 - HRB											18.00
68 - İBG										13.00	56.00
69 - Rannis											2.00
70 - IMAGINE					14.00					3.00	49.00
71 - IGC PAN											6.00
72 - ISCIII										2.00	76.00
73 - INSA											12.00
74 - IOR											3.00
75 - ISS				2.00						9.00	11.00
76 - IT-MOH											2.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP11	WP12	WP13	WP14	WP15	WP16	WP17	WP18	WP19	WP20	Total Person-Months
77 - KU Leuven											53.00
78 - LZP											2.00
79 - MRT						27.00					27.00
80 - MUS											6.00
81 - MUH											36.00
82 - MUR											2.00
83 - NCBR											2.00
84 - NKUA											6.00
85 - MoH SR											12.00
86 - RDG											8.00
87 - REGIONSYD											18.00
88 - OPBG											21.00
89 - OSR											43.00
90 - JSI											8.00
91 - RCN											2.00
92 - FWO											2.00
93 - REUH											21.00
94 - RIF											6.00
95 - RCSI											9.00
96 - RSU										2.00	5.00
97 - Sciensano											48.00

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP11	WP12	WP13	WP14	WP15	WP16	WP17	WP18	WP19	WP20	Total Person-Months
98 - SPW											2.00
99 - SFU									5.00	21.00	26.00
100 - ETAg											2.00
101 - SAS											2.00
102 - Sonio						27.00					27.00
103 - MOSAE											2.00
104 - SRC											2.00
105 - TEDDY										6.00	6.00
106 - TEKKARE											66.00
107 - TIF											12.00
108 - TUBITAK											6.00
109 - RT (TuscReg)											3.00
110 - UAB											20.00
111 - UCD										2.00	7.00
112 - UCSC										16.00	16.00
113 - UEF											27.00
114 - UKA									22.00		22.00
115 - UKLFR											38.00
116 - UNICAMPANIA											9.00
117 - UoC											6.00
118 - UGENT											24.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP11	WP12	WP13	WP14	WP15	WP16	WP17	WP18	WP19	WP20	Total Person-Months
119 - UKCL											9.00
120 - WDO										9.00	21.00
121 - UU					22.00				22.00		62.00
122 - c4c-S										10.00	10.00
123 - CAU											8.00
124 - CNRS											20.00
125 - CIBER											27.00
126 - UEFISCDI											2.00
127 - UNIROMA1										9.00	9.00
128 - UANTWERPEN											6.00
129 - BNSF											2.00
130 - Aalborg UH											6.00
131 - RDB											3.00
132 - BBMRI-ERIC			8.00								8.00
133 - AarhusUH											9.00
134 - IABS-EU								12.00			12.00
135 - HRCI											5.00
136.1 - KUM											41.00
137 - MSW											38.00
138 - FNR											2.00
139 - NKFIH											2.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP11	WP12	WP13	WP14	WP15	WP16	WP17	WP18	WP19	WP20	Total Person-Months
140 - PEI											36.00
141 - PLUS									22.00		37.00
142 - SU										2.00	3.00
143 - UNISI											9.00
144 - Vinnova											2.00
145 - CRG-CERCA				3.00							18.00
146 - GMS-RS											4.00
147 - VIB											3.00
148 - IPG											6.00
149 - UO											6.00
150 - HSJD											7.00
Total Person-Months	210.00	82.00	230.00	168.00	224.00	250.00	38.00	88.00	158.00	318.00	6355.00

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP21	WP22	WP23	WP24	WP25	WP26	Total Person-Months
1 - INSERM	12.00		152.00				828.00
1.1 - CAD							72.00
2 - TEAMIT					18.00		126.00
3 - DLR							31.00
4 - ANR							23.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP21	WP22	WP23	WP24	WP25	WP26	Total Person-Months
5 - FTELE	11.00						66.00
6 - LMT							6.00
7 - ZonMw			12.00	4.00	9.00		44.00
8 - UT							300.00
9 - UTARTU			12.00				56.00
10 - CNAG							278.00
11 - SRUMC		3.00					356.00
12 - TUM							84.00
13 - UKHD	3.00						279.00
14 - C-PATH							107.00
15 - VHIR	13.00						134.00
16 - LUMC							118.00
17 - UTWENTE							38.00
18 - UPM							149.00
19 - UMCG							166.00
20 - AUMC					1.00		67.00
21 - UM							36.00
22 - EATRIS		36.00					86.00
23 - FGB							93.00
24 - APHP							169.00
25 - UHASSELT							35.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP21	WP22	WP23	WP24	WP25	WP26	Total Person-Months
26 - EURORDIS		6.00		11.00	1.00		124.00
27 - VULSK			12.00	15.00			100.00
28 - UC	57.00						57.00
29 - FFRD		36.00		7.00	90.00		146.00
30 - AFM		36.00					44.00
31 - CCUH			30.00				30.00
32 - AICIB				19.00	1.00		23.00
33 - IMGGE				15.00			15.00
34 - RDI					12.00		19.00
35 - ACU							2.00
36 - AIT							23.00
37 - AMU							26.00
38 - AOU Meyer IRCCS							9.00
39 - ASU-FC					10.00		35.00
40 - BIU	3.00						3.00
42 - CCRI GmbH			12.00				36.00
43 - CENTOGENE							18.00
44 - CHARITE	61.00						61.00
45 - CHI	20.00						20.00
46 - CHU Dijon							27.00
47 - CE							54.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP21	WP22	WP23	WP24	WP25	WP26	Total Person-Months
48 - REGIONH							18.00
49 - CSO-MOH							21.00
50 - CVBF				5.00			31.00
51 - DDF							44.00
53 - Erasmus MC							68.00
54 - F.R.S.-FNRS							2.00
55 - FHG	62.00						62.00
56 - FRRB							2.00
57 - ECRIN							5.00
58 - FWF							2.00
59 - IFD							2.00
60 - FSJD-CERCA	23.00						23.00
61 - FCT							2.00
62.1 - AZV							2.00
63 - GNT	54.00						102.00
64 - GERAD				5.00			5.00
65 - RS							4.00
66 - GUF							11.00
67 - HRB			12.00	4.00			18.00
68 - İBG			12.00	12.00			56.00
69 - Rannis							2.00

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP21	WP22	WP23	WP24	WP25	WP26	Total Person-Months
70 - IMAGINE	20.00						49.00
71 - IGC PAN							6.00
72 - ISCIII		8.00	12.00		1.00		76.00
73 - INSA			12.00				12.00
74 - IOR					3.00		3.00
75 - ISS							11.00
76 - IT-MOH							2.00
77 - KU Leuven	37.00						53.00
78 - LZP							2.00
79 - MRT							27.00
80 - MUS							6.00
81 - MUH			12.00				36.00
82 - MUR							2.00
83 - NCBR							2.00
84 - NKUA							6.00
85 - MoH SR			12.00				12.00
86 - RDG			8.00				8.00
87 - REGIONSYD							18.00
88 - OPBG							21.00
89 - OSR	43.00						43.00
90 - JSI			8.00				8.00

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP21	WP22	WP23	WP24	WP25	WP26	Total Person-Months
91 - RCN							2.00
92 - FWO							2.00
93 - REUH				12.00			21.00
94 - RIF				4.00			6.00
95 - RCSI							9.00
96 - RSU				3.00			5.00
97 - Sciensano							48.00
98 - SPW							2.00
99 - SFU							26.00
100 - ETAg							2.00
101 - SAS							2.00
102 - Sonio							27.00
103 - MOSAE							2.00
104 - SRC							2.00
105 - TEDDY							6.00
106 - TEKKARE							66.00
107 - TIF			12.00				12.00
108 - TUBITAK				4.00			6.00
109 - RT (TuscReg)							3.00
110 - UAB	20.00						20.00
111 - UCD				5.00			7.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP21	WP22	WP23	WP24	WP25	WP26	Total Person-Months
112 - UCSC							16.00
113 - UEF	27.00						27.00
114 - UKA							22.00
115 - UKLFR	8.00						38.00
116 - UNICAMPANIA							9.00
117 - UoC							6.00
118 - UGENT							24.00
119 - UKCL							9.00
120 - WDO							21.00
121 - UU							62.00
122 - c4c-S							10.00
123 - CAU				7.00	1.00		8.00
124 - CNRS	20.00						20.00
125 - CIBER	18.00						27.00
126 - UEFISCDI							2.00
127 - UNIROMA1							9.00
128 - UANTWERPEN							6.00
129 - BNSF							2.00
130 - Aalborg UH							6.00
131 - RDB				3.00			3.00
132 - BBMRI-ERIC							8.00

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Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP21	WP22	WP23	WP24	WP25	WP26	Total Person-Months
133 - AarhusUH							9.00
134 - IABS-EU							12.00
135 - HRCI							5.00
136.1 - KUM							41.00
137 - MSW							38.00
138 - FNR							2.00
139 - NKFIH							2.00
140 - PEI	36.00						36.00
141 - PLUS	15.00						37.00
142 - SU					1.00		3.00
143 - UNISI							9.00
144 - Vinnova							2.00
145 - CRG-CERCA							18.00
146 - GMS-RS							4.00
147 - VIB							3.00
148 - IPG							6.00
149 - UO							6.00
150 - HSJD					7.00		7.00
Total Person-Months	563.00	125.00	330.00	135.00	155.00	0.00	6355.00

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LIST OF DELIVERABLES

Deliverables

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D1.1	Data Management Plan	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	6
D1.2	Annual Work Plan Y2	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	9
D1.3	Annual Work Plan Y3	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	21
D1.4	Annual Work Plan Y4	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	33
D1.5	Annual Work Plan Y5	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	45
D1.6	Annual Work Plan Y6	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	57
D1.7	Annual Work Plan Y7	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	69
D1.8	Periodic Progress Report 1	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	26
D1.9	Periodic Progress Report 2	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	44
D1.10	Periodic Progress Report 3	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	62
D1.11	Periodic Progress Report 4	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	74
D1.12	Periodic Progress Report 5	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	84
D1.13	RDP SRIA Update	WP1	1 - INSERM	R — Document, report	PU - Public	36
D1.14	Report on cumulative expenditure incurred	WP1	1 - INSERM	R — Document, report	SEN - Sensitive	12

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D2.1	Project website	WP2	2 - TEAMIT	DEC —Websites, patent filings, videos, etc	PU - Public	3
D2.2	Communication and dissemination strategy	WP2	2 - TEAMIT	R — Document, report	SEN - Sensitive	6
D3.1	Joint Transnational Call documents 1	WP3	3 - DLR	R — Document, report	SEN - Sensitive	3
D3.2	Joint Transnational Call documents 2	WP3	3 - DLR	R — Document, report	SEN - Sensitive	15
D3.3	Joint Transnational Call documents 3	WP3	3 - DLR	R — Document, report	SEN - Sensitive	27
D3.4	Joint Transnational Call documents 4	WP3	3 - DLR	R — Document, report	SEN - Sensitive	39
D3.5	Joint Transnational Call documents 5	WP3	3 - DLR	R — Document, report	SEN - Sensitive	51
D3.6	Joint Transnational Call documents 6	WP3	3 - DLR	R — Document, report	SEN - Sensitive	63
D3.7	Joint Transnational Call documents 7	WP3	3 - DLR	R — Document, report	SEN - Sensitive	75
D3.8	Evaluation Report of the JTCs 1	WP3	3 - DLR	R — Document, report	SEN - Sensitive	15
D3.9	Evaluation Report of the JTCs 2	WP3	3 - DLR	R — Document, report	SEN - Sensitive	27
D3.10	Evaluation Report of the JTCs 3	WP3	3 - DLR	R — Document, report	SEN - Sensitive	39
D3.11	Evaluation Report of the JTCs 4	WP3	3 - DLR	R — Document, report	SEN - Sensitive	51
D3.12	Evaluation Report of the JTCs 5	WP3	3 - DLR	R — Document, report	SEN - Sensitive	63
D3.13	Evaluation Report of the JTCs 6	WP3	3 - DLR	R — Document, report	SEN - Sensitive	75
D3.14	Evaluation Report of the JTCs 7	WP3	3 - DLR	R — Document, report	SEN - Sensitive	84

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D4.1	Clinical Trial Call documents	WP4	5 - FTELE	R — Document, report	PU - Public	18
D4.2	Evaluation Report of the Clinical Trial Call	WP4	5 - FTELE	R — Document, report	SEN - Sensitive	36
D5.1	NSS Call documents	WP5	7 - ZonMw	R — Document, report	SEN - Sensitive	9
D5.2	List of funded networks 1	WP5	7 - ZonMw	R — Document, report	PU - Public	36
D5.3	List of funded networks 2	WP5	7 - ZonMw	R — Document, report	PU - Public	84
D6.1	Roadmap for genomic federated data analysis approach	WP6	8 - UT	R — Document, report	PU - Public	6
D6.2	Research dataset on returned diagnostic results 1	WP6	8 - UT	R — Document, report	PU - Public	36
D6.3	Research dataset on returned diagnostic results 2	WP6	8 - UT	R — Document, report	PU - Public	84
D7.1	Coordinated re-analysis diagnostic pipeline	WP7	10 - CNAG	R — Document, report	PU - Public	12
D7.2	Best practice guidelines for diagnostic re-analysis & reinterpretation strategies	WP7	77 - KU Leuven	R — Document, report	PU - Public	30
D8.1	Software for long-read pipelines optimized for RD diagnoses	WP8	11 - SRUMC	OTHER	PU - Public	36
D8.2	Software update for integrated DNARNA pipeline optimized for RD discoveries 1	WP8	12 - TUM	OTHER	PU - Public	24

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D8.3	Software update for integrated DNARNA pipeline optimized for RD discoveries 2	WP8	12 - TUM	OTHER	PU - Public	60
D8.4	Software for multi-omics pipeline optimized for RD discoveries 1	WP8	37 - AMU	OTHER	PU - Public	36
D8.5	Software for multi-omics pipeline optimized for RD discoveries 2	WP8	37 - AMU	OTHER	PU - Public	72
D9.1	Regulatory grade cohort Inventory	WP9	136 - LMU	R — Document, report	PU - Public	36
D9.2	Individual disease progression models	WP9	8 - UT	R — Document, report	PU - Public	36
D9.3	Drug Development Tools	WP9	14 - C-PATH	R — Document, report	PU - Public	72
D10.1	Disease burden and cost of illness framework for RDs	WP10	97 - Sciensano	R — Document, report	PU - Public	36
D10.2	Platform for development of regulatorygrade patient-relevant COAs in RD	WP10	13 - UKHD	R — Document, report	PU - Public	84
D10.3	Toolbox on collection of patient selfreported data	WP10	15 - VHIR	R — Document, report	PU - Public	84
D11.1	Result of the PoC studies for ATMP technologies	WP11	1 - INSERM	DEM — Demonstrator, pilot, prototype	SEN - Sensitive	60
D11.2	ATMP technology Platform validated in clinical context	WP11	5 - FTELE	DEM — Demonstrator, pilot, prototype	PU - Public	84

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D12.1	Assessment criteria for patient eligibility to individualised ASO treatment	WP12	16 - LUMC	R — Document, report	SEN - Sensitive	36
D12.2	Toolkit on outcome measures for N-of- 1	WP12	8 - UT	DEC —Websites, patent filings, videos, etc	PU - Public	56
D12.3	Standardized platform for timely development of ASO individualized treatments	WP12	16 - LUMC	DEM — Demonstrator, pilot, prototype	PU - Public	84
D13.1	VP specifications and documentation 1	WP13	1 - INSERM	R — Document, report	PU - Public	12
D13.2	VP specifications and documentation 2	WP13	1 - INSERM	R — Document, report	PU - Public	36
D13.3	VP specifications and documentation 3	WP13	1 - INSERM	R — Document, report	PU - Public	84
D14.1	Data Stewardship Wizard with the compilation of data models and data preparation workflows 1	WP14	16 - LUMC	OTHER	PU - Public	12
D14.2	Data Stewardship Wizard with the compilation of data models and data preparation workflows 2	WP14	16 - LUMC	OTHER	PU - Public	36
D14.3	Data Stewardship Wizard with the compilation of data models and data preparation workflows 3	WP14	16 - LUMC	OTHER	PU - Public	84

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D15.1	Portfolio of ERDERA large scale analysis services and pipelines	WP15	19 - UMCG	DEC —Websites, patent filings, videos, etc	PU - Public	12
D15.2	Portfolio of ERDERA federated analysis methods and services	WP15	18 - UPM	DEC —Websites, patent filings, videos, etc	PU - Public	24
D15.3	Technical guidelines for the implementation of services used in the use cases on federated analysis	WP15	10 - CNAG	OTHER	PU - Public	30
D16.1	First standard application of multidimensional knowledge networks (RD maps) addressing an RD case	WP16	21 - UM	DEM — Demonstrator, pilot, prototype	PU - Public	36
D16.2	First version of ontologies (antenatal phenotypes and functional impacts) integrated with ORDO	WP16	1 - INSERM	DEM — Demonstrator, pilot, prototype	PU - Public	36
D16.3	Treatabolome demonstrator	WP16	1 - INSERM	DEM — Demonstrator, pilot, prototype	PU - Public	72
D16.4	Knowledge bases and ontologies for PROM/ PCOM, disabilities and Treatabolome	WP16	1 - INSERM	DEM — Demonstrator, pilot, prototype	PU - Public	84
D17.1	Recommendations to funders on addressing translatability of projects through funding opportunities	WP17	22 - EATRIS	R — Document, report	SEN - Sensitive	36

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D17.2	Result of feasibility study for consultancy-based expertise services	WP17	23 - FGB	R — Document, report	SEN - Sensitive	36
D17.3	Final report of the mentoring services activity	WP17	22 - EATRIS	R — Document, report	SEN - Sensitive	84
D18.1	Set of regulatory recommendations for CRNs	WP18	23 - FGB	R — Document, report	SEN - Sensitive	6
D18.2	Set of Regulatory support tools for preclinical development to facilitate regulatory filings and convergence for RD	WP18	22 - EATRIS	R — Document, report	PU - Public	36
D18.3	Roadmap for physical and written standards for quality control of ATMPs	WP18	22 - EATRIS	R — Document, report	SEN - Sensitive	60
D18.4	Summary report of ERDERA Qualification applications with regulatory Authorities	WP18	23 - FGB	R — Document, report	PU - Public	80
D19.1	First knowledge transfer of protocols & tools to CRN and selected JTC projects	WP19	24 - APHP	OTHER	PU - Public	36
D19.2	Final knowledge transfer of protocols & tools to CRN and selected JTC projects	WP19	24 - APHP	OTHER	PU - Public	84
D19.3	First protocol & tools for methodological upscaling of RD research projects	WP19	25 - UHASSELT	OTHER	PU - Public	36

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D19.4	Final protocol & tools for methodological upscaling of RD research projects	WP19	25 - UHASSELT	OTHER	PU - Public	84
D20.1	Report on the identification and fulfilment of RD education and training needs	WP20	27 - VULSK	R — Document, report	PU - Public	36
D20.2	Impact assessment of ERDERA education and training programme	WP20	27 - VULSK	R — Document, report	PU - Public	84
D21.1	Base protocols for research grade rAAVs production	WP21	63 - GNT	R — Document, report	PU - Public	25
D21.2	Computational tools for of LNPs, EVs and biohybrids formulation development	WP21	164 - RJF	OTHER	SEN - Sensitive	30
D21.3	gRNAs for effective and safe gene editing	WP21	70 - IMAGINE	R — Document, report	SEN - Sensitive	36
D21.4	Dataset of Gene therapy Immunogenicity assessment on humanized mouse model	WP21	1 - INSERM	DATA — data sets, microdata, etc	PU - Public	36
D21.5	Multiomics single cell analysis and bioinformatic pipeline fit-for-purpose qualified to characterize immune response to ATMPs	WP21	45 - CHI	DATA — data sets, microdata, etc	SEN - Sensitive	36
D21.6	Report on standard regulatory quality control parameters of mRNA formulations	WP21	161 - Pfizer	R — Document, report	PU - Public	50

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D21.7	Regulatory compliant recommendations for rAAV analytics	WP21	77 - KU Leuven	R — Document, report	PU - Public	58
D22.1	Accelerator Hub inclusion criteria for research projects	WP22	30 - AFM	R — Document, report	SEN - Sensitive	12
D22.2	Impact analysis of Accelerator hub outputs 1	WP22	22 - EATRIS	R — Document, report	PU - Public	36
D22.3	Impact analysis of Accelerator hub outputs 2	WP22	22 - EATRIS	R — Document, report	PU - Public	84
D23.1	Best practice guidelines for creation and promotion of NMGs	WP23	1 - INSERM	R — Document, report	PU - Public	6
D23.2	First report on the impact of NMGs	WP23	170 - UNEW	R — Document, report	PU - Public	36
D23.3	Second report on the impact of NMGs	WP23	170 - UNEW	R — Document, report	PU - Public	80
D23.4	Recommendations on the NMG sustainability	WP23	31 - CCUH	R — Document, report	PU - Public	77
D24.1	Mapping of UCs specific needs and expectations 1	WP24	27 - VULSK	R — Document, report	SEN - Sensitive	12
D24.2	Mapping of UCs specific needs and expectations 2	WP24	27 - VULSK	R — Document, report	SEN - Sensitive	48
D24.3	Focused guidelines for actions at the National level 1	WP24	93 - REUH	R — Document, report	PU - Public	24

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D24.4	Focused guidelines for actions at the National level 2	WP24	93 - REUH	R — Document, report	PU - Public	48
D24.5	Guidelines to increase UCs integration in ERDERA (including in funding activities) 1	WP24	32 - AICIB	R — Document, report	PU - Public	12
D24.6	Guidelines to increase UCs integration in ERDERA (including in funding activities) 2	WP24	32 - AICIB	R — Document, report	PU - Public	48
D24.7	Guidelines to increase UCs integration in ERDERA (including in funding activities) 3	WP24	32 - AICIB	R — Document, report	PU - Public	72
D25.1	White paper on ERNs Living Lab 1	WP25	39 - ASU-FC	R — Document, report	PU - Public	36
D25.2	White paper on ERNs Living Lab 2	WP25	39 - ASU-FC	R — Document, report	PU - Public	84
D25.3	Sustainability Plan for established strategic alliances and partnerships	WP25	7 - ZonMw	DEM — Demonstrator, pilot, prototype	SEN - Sensitive	75
D25.4	Publication on the International CRNs	WP25	34 - RDI	R — Document, report	PU - Public	84
D26.1	OEI - Requirement No. 1	WP26	1 - INSERM	ETHICS	SEN - Sensitive	1
D26.2	OEI - Requirement No. 2	WP26	1 - INSERM	ETHICS	SEN - Sensitive	12
D26.3	OEI - Requirement No. 3	WP26	1 - INSERM	ETHICS	SEN - Sensitive	24
D26.4	OEI - Requirement No. 4	WP26	1 - INSERM	ETHICS	SEN - Sensitive	36
D26.5	OEI - Requirement No. 5	WP26	1 - INSERM	ETHICS	SEN - Sensitive	48

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D26.6	OEI - Requirement No. 6	WP26	1 - INSERM	ETHICS	SEN - Sensitive	60
D26.7	OEI - Requirement No. 7	WP26	1 - INSERM	ETHICS	SEN - Sensitive	72
D26.8	OEI - Requirement No. 8	WP26	1 - INSERM	ETHICS	SEN - Sensitive	84

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Deliverable D1.1 – Data Management Plan

Deliverable Number	D1.1	Lead Beneficiary	1 - INSERM
Deliverable Name	Data Management Plan		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	6	Work Package No	WP1

Description
Detailed data management plan. To be constantly updated, and the resulting version will be submitted at each reporting period.

Deliverable D1.2 – Annual Work Plan Y2

Deliverable Number	D1.2	Lead Beneficiary	1 - INSERM
Deliverable Name	Annual Work Plan Y2		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	9	Work Package No	WP1

Description
Detailing the planned activities and resources.

Deliverable D1.3 – Annual Work Plan Y3

Deliverable Number	D1.3	Lead Beneficiary	1 - INSERM
Deliverable Name	Annual Work Plan Y3		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	21	Work Package No	WP1

Description
Detailing the planned activities and resources.

Deliverable D1.4 – Annual Work Plan Y4

Deliverable Number	D1.4	Lead Beneficiary	1 - INSERM
Deliverable Name	Annual Work Plan Y4		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	33	Work Package No	WP1

Description
Detailing the planned activities and resources.

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Deliverable D1.5 – Annual Work Plan Y5

Deliverable Number	D1.5	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Annual Work Plan Y5		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	45	**Work Package No**	WP1

Description
Detailing the planned activities and resources.

Deliverable D1.6 – Annual Work Plan Y6

Deliverable Number	D1.6	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Annual Work Plan Y6		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	57	**Work Package No**	WP1

Description
Detailing the planned activities and resources.

Deliverable D1.7 – Annual Work Plan Y7

Deliverable Number	D1.7	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Annual Work Plan Y7		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	69	**Work Package No**	WP1

Description
Detailing the planned activities and resources.

Deliverable D1.8 – Periodic Progress Report 1

Deliverable Number	D1.8	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Periodic Progress Report 1		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	26	**Work Package No**	WP1

Description
ERDERA progress report.

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Deliverable D1.9 – Periodic Progress Report 2

Deliverable Number	D1.9	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Periodic Progress Report 2		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	44	**Work Package No**	WP1

Description
ERDERA progress report.

Deliverable D1.10 – Periodic Progress Report 3

Deliverable Number	D1.10	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Periodic Progress Report 3		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	62	**Work Package No**	WP1

Description
ERDERA progress report.

Deliverable D1.11 – Periodic Progress Report 4

Deliverable Number	D1.11	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Periodic Progress Report 4		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	74	**Work Package No**	WP1

Description
ERDERA progress report.

Deliverable D1.12 – Periodic Progress Report 5

Deliverable Number	D1.12	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Periodic Progress Report 5		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	84	**Work Package No**	WP1

Description
ERDERA progress report.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D1.13 – RDP SRIA Update

Deliverable Number	D1.13	Lead Beneficiary	1 - INSERM
Deliverable Name	RDP SRIA Update		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	36	Work Package No	WP1

Description
ERDERA SRIA updated

Deliverable D1.14 – Report on cumulative expenditure incurred

Deliverable Number	D1.14	Lead Beneficiary	1 - INSERM
Deliverable Name	Report on cumulative expenditure incurred		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	12	Work Package No	WP1

Description
Report on cumulative expenditure incurred.

Deliverable D2.1 – Project website

Deliverable Number	D2.1	Lead Beneficiary	2 - TEAMIT
Deliverable Name	Project website		
Type	DEC —Websites, patent filings, videos, etc	Dissemination Level	PU - Public
Due Date (month)	3	Work Package No	WP2

Description
Report on ERDERA visual identity manual and website development.

Deliverable D2.2 – Communication and dissemination strategy

Deliverable Number	D2.2	Lead Beneficiary	2 - TEAMIT
Deliverable Name	Communication and dissemination strategy		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	6	Work Package No	WP2

Description
Audience analysis, objectives; key messages; channels & tools; KPIs, initial plan.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D3.1 – Joint Transnational Call documents 1

Deliverable Number	D3.1	Lead Beneficiary	3 - DLR
Deliverable Name	Joint Transnational Call documents 1		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	3	Work Package No	WP3

Description
Report including MoU, call text, guidelines, application's form templates.

Deliverable D3.2 – Joint Transnational Call documents 2

Deliverable Number	D3.2	Lead Beneficiary	3 - DLR
Deliverable Name	Joint Transnational Call documents 2		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	15	Work Package No	WP3

Description
Report including MoU, call text, guidelines, application's form templates.

Deliverable D3.3 – Joint Transnational Call documents 3

Deliverable Number	D3.3	Lead Beneficiary	3 - DLR
Deliverable Name	Joint Transnational Call documents 3		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	27	Work Package No	WP3

Description
Report including MoU, call text, guidelines, application's form templates.

Deliverable D3.4 – Joint Transnational Call documents 4

Deliverable Number	D3.4	Lead Beneficiary	3 - DLR
Deliverable Name	Joint Transnational Call documents 4		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	39	Work Package No	WP3

Description
Report including MoU, call text, guidelines, application's form templates.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D3.5 – Joint Transnational Call documents 5

Deliverable Number	D3.5	**Lead Beneficiary**	3 - DLR
Deliverable Name	Joint Transnational Call documents 5		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	51	**Work Package No**	WP3

Description
Report including MoU, call text, guidelines, application's form templates.

Deliverable D3.6 – Joint Transnational Call documents 6

Deliverable Number	D3.6	**Lead Beneficiary**	3 - DLR
Deliverable Name	Joint Transnational Call documents 6		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	63	**Work Package No**	WP3

Description
Report including MoU, call text, guidelines, application's form templates.

Deliverable D3.7 – Joint Transnational Call documents 7

Deliverable Number	D3.7	**Lead Beneficiary**	3 - DLR
Deliverable Name	Joint Transnational Call documents 7		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	75	**Work Package No**	WP3

Description
Report including MoU, call text, guidelines, application's form templates.

Deliverable D3.8 – Evaluation Report of the JTCs 1

Deliverable Number	D3.8	**Lead Beneficiary**	3 - DLR
Deliverable Name	Evaluation Report of the JTCs 1		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	15	**Work Package No**	WP3

Description
Report including the observers' report on the evaluation, the joint selection list of the projects to be funded.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D3.9 – Evaluation Report of the JTCs 2

Deliverable Number	D3.9	**Lead Beneficiary**	3 - DLR
Deliverable Name	Evaluation Report of the JTCs 2		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	27	**Work Package No**	WP3

Description
Report including the observers' report on the evaluation, the joint selection list of the projects to be funded.

Deliverable D3.10 – Evaluation Report of the JTCs 3

Deliverable Number	D3.10	**Lead Beneficiary**	3 - DLR
Deliverable Name	Evaluation Report of the JTCs 3		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	39	**Work Package No**	WP3

Description
Report including the observers' report on the evaluation, the joint selection list of the projects to be funded.

Deliverable D3.11 – Evaluation Report of the JTCs 4

Deliverable Number	D3.11	**Lead Beneficiary**	3 - DLR
Deliverable Name	Evaluation Report of the JTCs 4		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	51	**Work Package No**	WP3

Description
Report including the observers' report on the evaluation, the joint selection list of the projects to be funded.

Deliverable D3.12 – Evaluation Report of the JTCs 5

Deliverable Number	D3.12	**Lead Beneficiary**	3 - DLR
Deliverable Name	Evaluation Report of the JTCs 5		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	63	**Work Package No**	WP3

Description
Report including the observers' report on the evaluation, the joint selection list of the projects to be funded.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D3.13 – Evaluation Report of the JTCs 6

Deliverable Number	D3.13	**Lead Beneficiary**	3 - DLR
Deliverable Name	Evaluation Report of the JTCs 6		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	75	**Work Package No**	WP3

Description
Report including the observers' report on the evaluation, the joint selection list of the projects to be funded.

Deliverable D3.14 – Evaluation Report of the JTCs 7

Deliverable Number	D3.14	**Lead Beneficiary**	3 - DLR
Deliverable Name	Evaluation Report of the JTCs 7		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	84	**Work Package No**	WP3

Description
Report including the observers' report on the evaluation, the joint selection list of the projects to be funded.

Deliverable D4.1 – Clinical Trial Call documents

Deliverable Number	D4.1	**Lead Beneficiary**	5 - FTELE
Deliverable Name	Clinical Trial Call documents		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	18	**Work Package No**	WP4

Description
Supporting documentation, application form, guidelines for applicants, data, privacy and regulations

Deliverable D4.2 – Evaluation Report of the Clinical Trial Call

Deliverable Number	D4.2	**Lead Beneficiary**	5 - FTELE
Deliverable Name	Evaluation Report of the Clinical Trial Call		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP4

Description
Report including the observers' report on the evaluation, the list of the projects to be funded

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D5.1 – NSS Call documents

Deliverable Number	D5.1	Lead Beneficiary	7 - ZonMw
Deliverable Name	NSS Call documents		
Type	R — Document, report	Dissemination Level	SEN - Sensitive
Due Date (month)	9	Work Package No	WP5

Description
Supporting documentation (call text, application template, confidential document for evaluators)

Deliverable D5.2 – List of funded networks 1

Deliverable Number	D5.2	Lead Beneficiary	7 - ZonMw
Deliverable Name	List of funded networks 1		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	36	Work Package No	WP5

Description
List of the networks selected for funding, including summaries

Deliverable D5.3 – List of funded networks 2

Deliverable Number	D5.3	Lead Beneficiary	7 - ZonMw
Deliverable Name	List of funded networks 2		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	84	Work Package No	WP5

Description
List of the networks selected for funding, including summaries

Deliverable D6.1 – Roadmap for genomic federated data analysis approach

Deliverable Number	D6.1	Lead Beneficiary	8 - UT
Deliverable Name	Roadmap for genomic federated data analysis approach		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	6	Work Package No	WP6

Description
Strategy agreed with 1+MG/GDI from the joint workshop

Deliverable D6.2 – Research dataset on returned diagnostic results 1

Deliverable Number	D6.2	**Lead Beneficiary**	8 - UT
Deliverable Name	Research dataset on returned diagnostic results 1		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP6

Description
Aggregated data processed to generate returned diagnostic results

Deliverable D6.3 – Research dataset on returned diagnostic results 2

Deliverable Number	D6.3	**Lead Beneficiary**	8 - UT
Deliverable Name	Research dataset on returned diagnostic results 2		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP6

Description
Aggregated data processed to generate returned diagnostic results

Deliverable D7.1 – Coordinated re-analysis diagnostic pipeline

Deliverable Number	D7.1	**Lead Beneficiary**	10 - CNAG
Deliverable Name	Coordinated re-analysis diagnostic pipeline		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	12	**Work Package No**	WP7

Description
Description of the revised coordinated re-analysis research diagnostic pipeline

Deliverable D7.2 – Best practice guidelines for diagnostic re-analysis & reinterpretation strategies

Deliverable Number	D7.2	**Lead Beneficiary**	77 - KU Leuven
Deliverable Name	Best practice guidelines for diagnostic re-analysis & reinterpretation strategies		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	30	**Work Package No**	WP7

Description
Translation of successful diagnostic reanalysis strategies into best practice guidelines, including the propagation and evaluation of phenotypic and ontology usage

Deliverable D8.1 – Software for long-read pipelines optimized for RD diagnoses

Deliverable Number	D8.1	**Lead Beneficiary**	11 - SRUMC
Deliverable Name	Software for long-read pipelines optimized for RD diagnoses		
Type	OTHER	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP8

Description
Software for ONT and PacBio sequencing to call most variant types released, tested and optimized for RD use

Deliverable D8.2 – Software update for integrated DNARNA pipeline optimized for RD discoveries 1

Deliverable Number	D8.2	**Lead Beneficiary**	12 - TUM
Deliverable Name	Software update for integrated DNARNA pipeline optimized for RD discoveries 1		
Type	OTHER	**Dissemination Level**	PU - Public
Due Date (month)	24	**Work Package No**	WP8

Description
Software (update) released for an integrated DNA-RNA analysis of RD data released, tested and optimized for RD use

Deliverable D8.3 – Software update for integrated DNARNA pipeline optimized for RD discoveries 2

Deliverable Number	D8.3	**Lead Beneficiary**	12 - TUM
Deliverable Name	Software update for integrated DNARNA pipeline optimized for RD discoveries 2		
Type	OTHER	**Dissemination Level**	PU - Public
Due Date (month)	60	**Work Package No**	WP8

Description
Software (update) released for an integrated DNA-RNA analysis of RD data released, tested and optimized for RD use

Deliverable D8.4 – Software for multi-omics pipeline optimized for RD discoveries 1

Deliverable Number	D8.4	**Lead Beneficiary**	37 - AMU
Deliverable Name	Software for multi-omics pipeline optimized for RD discoveries 1		
Type	OTHER	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP8

Description
Software released for an integrated multi-omics RD data released, tested and optimized for RD use

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D8.5 – Software for multi-omics pipeline optimized for RD discoveries 2

Deliverable Number	D8.5	**Lead Beneficiary**	37 - AMU
Deliverable Name	Software for multi-omics pipeline optimized for RD discoveries 2		
Type	OTHER	**Dissemination Level**	PU - Public
Due Date (month)	72	**Work Package No**	WP8

Description
Software released for an integrated multi-omics RD data released, tested and optimized for RD use

Deliverable D9.1 – Regulatory grade cohort Inventory

Deliverable Number	D9.1	**Lead Beneficiary**	136 - LMU
Deliverable Name	Regulatory grade cohort Inventory		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP9

Description
Online list of EMA approved RD cohort data sets

Deliverable D9.2 – Individual disease progression models

Deliverable Number	D9.2	**Lead Beneficiary**	8 - UT
Deliverable Name	Individual disease progression models		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP9

Description
4 pilot models for individual-subject progression modelling and prediction

Deliverable D9.3 – Drug Development Tools

Deliverable Number	D9.3	**Lead Beneficiary**	14 - C-PATH
Deliverable Name	Drug Development Tools		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	72	**Work Package No**	WP9

Description
Two drug development tools established and accepted by EMA

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D10.1 – Disease burden and cost of illness framework for RDs

Deliverable Number	D10.1	**Lead Beneficiary**	97 - Sciensano
Deliverable Name	Disease burden and cost of illness framework for RDs		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP10

Description
Framework to estimate cost of illness and burden of disease (BoD) in case data for other RDs becomes available

Deliverable D10.2 – Platform for development of regulatorygrade patient-relevant COAs in RD

Deliverable Number	D10.2	**Lead Beneficiary**	13 - UKHD
Deliverable Name	Platform for development of regulatorygrade patient-relevant COAs in RD		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP10

Description
Step-by-step description of COAs development process

Deliverable D10.3 – Toolbox on collection of patient selfreported data

Deliverable Number	D10.3	**Lead Beneficiary**	15 - VHIR
Deliverable Name	Toolbox on collection of patient selfreported data		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP10

Description
Pragmatic guidance on data standardization, regulatory and technological aspects for implementing patient selfreported data in clinical studies

Deliverable D11.1 – Result of the PoC studies for ATMP technologies

Deliverable Number	D11.1	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Result of the PoC studies for ATMP technologies		
Type	DEM — Demonstrator, pilot, prototype	**Dissemination Level**	SEN - Sensitive
Due Date (month)	60	**Work Package No**	WP11

Description
Proof-of-concept studies to support efficacy of the chosen technology on relevant preclinical models of the identified diseases

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D11.2 – ATMP technology Platform validated in clinical context

Deliverable Number	D11.2	**Lead Beneficiary**	5 - FTELE
Deliverable Name	ATMP technology Platform validated in clinical context		
Type	DEM — Demonstrator, pilot, prototype	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP11

Description
Evaluation of the clinical translatability of the technology platform in the context of the selected disease

Deliverable D12.1 – Assessment criteria for patient eligibility to individualised ASO treatment

Deliverable Number	D12.1	**Lead Beneficiary**	16 - LUMC
Deliverable Name	Assessment criteria for patient eligibility to individualised ASO treatment		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP12

Description
Report on how to assess patient eligibility for individualized treatment (mutation, disease, patient and other considerations)

Deliverable D12.2 – Toolkit on outcome measures for N-of- 1

Deliverable Number	D12.2	**Lead Beneficiary**	8 - UT
Deliverable Name	Toolkit on outcome measures for N-of- 1		
Type	DEC —Websites, patent filings, videos, etc	**Dissemination Level**	PU - Public
Due Date (month)	56	**Work Package No**	WP12

Description
Catalogue of outcome measures available online

Deliverable D12.3 – Standardized platform for timely development of ASO individualized treatments

Deliverable Number	D12.3	**Lead Beneficiary**	16 - LUMC
Deliverable Name	Standardized platform for timely development of ASO individualized treatments		
Type	DEM — Demonstrator, pilot, prototype	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP12

Description

Operational platform for patient identification, ASO design and synthesis, safety assessment in cells and animals and ethics management

Deliverable D13.1 – VP specifications and documentation 1

Deliverable Number	D13.1	**Lead Beneficiary**	1 - INSERM
Deliverable Name	VP specifications and documentation 1		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	12	**Work Package No**	WP13

Description
First issue of a compilation of specifications, requirements, and documentations of the RD-VP, including onboarding guidance

Deliverable D13.2 – VP specifications and documentation 2

Deliverable Number	D13.2	**Lead Beneficiary**	1 - INSERM
Deliverable Name	VP specifications and documentation 2		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP13

Description
Intermediate issue of a compilation of specifications, requirements, and documentations of the RD-VP, including onboarding guidance

Deliverable D13.3 – VP specifications and documentation 3

Deliverable Number	D13.3	**Lead Beneficiary**	1 - INSERM
Deliverable Name	VP specifications and documentation 3		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP13

Description
Final issue of a compilation of specifications, requirements, and documentations of the RD-VP, including onboarding guidance

Deliverable D14.1 – Data Stewardship Wizard with the compilation of data models and data preparation workflows 1

Deliverable Number	D14.1	**Lead Beneficiary**	16 - LUMC
Deliverable Name	Data Stewardship Wizard with the compilation of data models and data preparation workflows 1		
Type	OTHER	**Dissemination Level**	PU - Public

Due Date (month)	12	Work Package No	WP14

Description
First issue of a compilation of data models and data ingestions pipelines (conversions, transformations, deposition options) disseminated as an updated version of the Data Stewardship Wizard

Deliverable D14.2 – Data Stewardship Wizard with the compilation of data models and data preparation workflows 2

Deliverable Number	D14.2	Lead Beneficiary	16 - LUMC
Deliverable Name	Data Stewardship Wizard with the compilation of data models and data preparation workflows 2		
Type	OTHER	Dissemination Level	PU - Public
Due Date (month)	36	Work Package No	WP14

Description
Intermediate issue of a compilation of data models and data ingestions pipelines (conversions, transformations, deposition options) disseminated as an updated version of the Data Stewardship Wizard

Deliverable D14.3 – Data Stewardship Wizard with the compilation of data models and data preparation workflows 3

Deliverable Number	D14.3	Lead Beneficiary	16 - LUMC
Deliverable Name	Data Stewardship Wizard with the compilation of data models and data preparation workflows 3		
Type	OTHER	Dissemination Level	PU - Public
Due Date (month)	84	Work Package No	WP14

Description
Final issue of a compilation of data models and data ingestions pipelines (conversions, transformations, deposition options) disseminated as an updated version of the Data Stewardship Wizard

Deliverable D15.1 – Portfolio of ERDERA large scale analysis services and pipelines

Deliverable Number	D15.1	Lead Beneficiary	19 - UMCG
Deliverable Name	Portfolio of ERDERA large scale analysis services and pipelines		
Type	DEC —Websites, patent filings, videos, etc	Dissemination Level	PU - Public
Due Date (month)	12	Work Package No	WP15

Description
Practical documentation for analysis service developers, operators and end-users on SOPs, templates, pipelines and services. It will be updated as necessary during the project

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D15.2 – Portfolio of ERDERA federated analysis methods and services

Deliverable Number	D15.2	**Lead Beneficiary**	18 - UPM
Deliverable Name	Portfolio of ERDERA federated analysis methods and services		
Type	DEC —Websites, patent filings, videos, etc	**Dissemination Level**	PU - Public
Due Date (month)	24	**Work Package No**	WP15

Description
Practical documentation for federated analysis service developers, operators and end-users

Deliverable D15.3 – Technical guidelines for the implementation of services used in the use cases on federated analysis

Deliverable Number	D15.3	**Lead Beneficiary**	10 - CNAG
Deliverable Name	Technical guidelines for the implementation of services used in the use cases on federated analysis		
Type	OTHER	**Dissemination Level**	PU - Public
Due Date (month)	30	**Work Package No**	WP15

Description
Description of the tools and methods used in the federated analyses use cases. It will be updated as necessary during the project

Deliverable D16.1 – First standard application of multidimensional knowledge networks (RD maps) addressing an RD case

Deliverable Number	D16.1	**Lead Beneficiary**	21 - UM
Deliverable Name	First standard application of multidimensional knowledge networks (RD maps) addressing an RD case		
Type	DEM — Demonstrator, pilot, prototype	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP16

Description
First multidimensional knowledge networks - spanning from genetic causes to observed phenotypes and treatment pathways developed and implemented in an RD case/application

Deliverable D16.2 – First version of ontologies (antenatal phenotypes and functional impacts) integrated with ORDO

Deliverable Number	D16.2	**Lead Beneficiary**	1 - INSERM
Deliverable Name	First version of ontologies (antenatal phenotypes and functional impacts) integrated with ORDO		

Type	DEM — Demonstrator, pilot, prototype	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP16

Description
Ontological models produced and populated with curated content and published in Orphadata

Deliverable D16.3 – Treatabolome demonstrator

Deliverable Number	D16.3	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Treatabolome demonstrator		
Type	DEM — Demonstrator, pilot, prototype	**Dissemination Level**	PU - Public
Due Date (month)	72	**Work Package No**	WP16

Description
Upscaled and expanded Treatabolome with additional disease groups and functionalities to facilitate data entry and data curation

Deliverable D16.4 – Knowledge bases and ontologies for PROM/PCOM, disabilities and Treatabolome

Deliverable Number	D16.4	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Knowledge bases and ontologies for PROM/PCOM, disabilities and Treatabolome		
Type	DEM — Demonstrator, pilot, prototype	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP16

Description
Completed knowledgebases – including interoperability (in RD maps) and inclusion in virtual platform

Deliverable D17.1 – Recommendations to funders on addressing translatability of projects through funding opportunities

Deliverable Number	D17.1	**Lead Beneficiary**	22 - EATRIS
Deliverable Name	Recommendations to funders on addressing translatability of projects through funding opportunities		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP17

Description
A document providing recommendations for the design of the calls based on the feedback of experts who provided support to the projects funded by ERDERA

Deliverable D17.2 – Result of feasibility study for consultancy-based expertise services

Deliverable Number	D17.2	**Lead Beneficiary**	23 - FGB
Deliverable Name	Result of feasibility study for consultancy-based expertise services		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP17

Description
Report describing the outcomes from the feasibility study on the proposed management and operations of the consultancy service

Deliverable D17.3 – Final report of the mentoring services activity

Deliverable Number	D17.3	**Lead Beneficiary**	22 - EATRIS
Deliverable Name	Final report of the mentoring services activity		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	84	**Work Package No**	WP17

Description
A report describing the result of the mentoring process

Deliverable D18.1 – Set of regulatory recommendations for CRNs

Deliverable Number	D18.1	**Lead Beneficiary**	23 - FGB
Deliverable Name	Set of regulatory recommendations for CRNs		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	6	**Work Package No**	WP18

Description
Set of regulatory recommendations processing of heath data and biosamples handling in clinical studies to prepare CRNs on a regulatory-compliant clinical research

Deliverable D18.2 – Set of Regulatory support tools for preclinical development to facilitate regulatory filings and convergence for RD

Deliverable Number	D18.2	**Lead Beneficiary**	22 - EATRIS
Deliverable Name	Set of Regulatory support tools for preclinical development to facilitate regulatory filings and convergence for RD		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP18

Description

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Report on prospective tools, standards methods, and resources, including a regulatory database to support regulatory filings and convergence for rare disease

Deliverable D18.3 – Roadmap for physical and written standards for quality control of ATMPs

Deliverable Number	D18.3	**Lead Beneficiary**	22 - EATRIS
Deliverable Name	Roadmap for physical and written standards for quality control of ATMPs		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	60	**Work Package No**	WP18

Description
Roadmap on how to realize the prioritized list of physical or written quality standards needed to support the platform technologies of the project

Deliverable D18.4 – Summary report of ERDERA Qualification applications with regulatory Authorities

Deliverable Number	D18.4	**Lead Beneficiary**	23 - FGB
Deliverable Name	Summary report of ERDERA Qualification applications with regulatory Authorities		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	80	**Work Package No**	WP18

Description
Final overview of status and required future steps, of qualification applications with Regulatory authorities for novel therapeutic approaches developed within the project

Deliverable D19.1 – First knowledge transfer of protocols & tools to CRN and selected JTC projects

Deliverable Number	D19.1	**Lead Beneficiary**	24 - APHP
Deliverable Name	First knowledge transfer of protocols & tools to CRN and selected JTC projects		
Type	OTHER	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP19

Description
First reports & tools (including software) describing the State-of-the art methodology and recommendations transferred to ERDERA funded and inhouse research project, including biostatistical, epidemiological, data science, artificial intelligence and machine learning dimensions

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D19.2 – Final knowledge transfer of protocols & tools to CRN and selected JTC projects

Deliverable Number	D19.2	**Lead Beneficiary**	24 - APHP
Deliverable Name	Final knowledge transfer of protocols & tools to CRN and selected JTC projects		
Type	OTHER	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP19

Description
Final reports & tools (including software) describing the State-of-the art methodology and recommendations transferred to ERDERA funded and inhouse research project, including biostatistical, epidemiological, data science, artificial intelligence and machine learning dimensions

Deliverable D19.3 – First protocol & tools for methodological upscaling of RD research projects

Deliverable Number	D19.3	**Lead Beneficiary**	25 - UHASSELT
Deliverable Name	First protocol & tools for methodological upscaling of RD research projects		
Type	OTHER	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP19

Description
First report & tools (including software) on the learnings and applications resulting from at least three conducted methodological projects

Deliverable D19.4 – Final protocol & tools for methodological upscaling of RD research projects

Deliverable Number	D19.4	**Lead Beneficiary**	25 - UHASSELT
Deliverable Name	Final protocol & tools for methodological upscaling of RD research projects		
Type	OTHER	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP19

Description
Final report & tools (including software) on the learnings and applications resulting from at least three conducted methodological projects

Deliverable D20.1 – Report on the identification and fulfilment of RD education and training needs

Deliverable Number	D20.1	**Lead Beneficiary**	27 - VULSK
Deliverable Name	Report on the identification and fulfilment of RD education and training needs		
Type	R — Document, report	**Dissemination Level**	PU - Public

Due Date (month)	36	Work Package No	WP20

Description
Evaluation of state-of-the-art of RD education and training in ERDERA and beyond

Deliverable D20.2 – Impact assessment of ERDERA education and training programme

Deliverable Number	D20.2	Lead Beneficiary	27 - VULSK
Deliverable Name	Impact assessment of ERDERA education and training programme		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	84	Work Package No	WP20

Description
Impact assessment of ERDERA education and training programme and further recommendations for continuous improvement

Deliverable D21.1 – Base protocols for research grade rAAVs production

Deliverable Number	D21.1	Lead Beneficiary	63 - GNT
Deliverable Name	Base protocols for research grade rAAVs production		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	25	Work Package No	WP21

Description
Development of base protocols for rAAV production based on publicly available, state-of-the-art knowledge & methodologies

Deliverable D21.2 – Computational tools for of LNPs, EVs and biohybrids formulation development

Deliverable Number	D21.2	Lead Beneficiary	164 - RJF
Deliverable Name	Computational tools for of LNPs, EVs and biohybrids formulation development		
Type	OTHER	Dissemination Level	SEN - Sensitive
Due Date (month)	30	Work Package No	WP21

Description
Development of computational tools for formulation development and running first test set

Deliverable D21.3 – gRNAs for effective and safe gene editing

Deliverable Number	D21.3	Lead Beneficiary	70 - IMAGINE
Deliverable Name	gRNAs for effective and safe gene editing		

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP21

Description
In vitro nomination of an effective and specific gene editing reagent for each of the selected rare diseases

Deliverable D21.4 – Dataset of Gene therapy Immunogenicity assessment on humanized mouse model

Deliverable Number	D21.4	**Lead Beneficiary**	1 - INSERM
Deliverable Name	Dataset of Gene therapy Immunogenicity assessment on humanized mouse model		
Type	DATA — data sets, microdata, etc	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP21

Description
Data set of complex immunogenicity results to at least four gene therapy tools in NSG-mice engrafted with human immune system

Deliverable D21.5 – Multiomics single cell analysis and bioinformatic pipeline fit-for-purpose qualified to characterize immune response to ATMPs

Deliverable Number	D21.5	**Lead Beneficiary**	45 - CHI
Deliverable Name	Multiomics single cell analysis and bioinformatic pipeline fit-for-purpose qualified to characterize immune response to ATMPs		
Type	DATA — data sets, microdata, etc	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP21

Description
Methodical and Bioinformatics workflow on multiomics analysis of immune therapy response

Deliverable D21.6 – Report on standard regulatory quality control parameters of mRNA formulations

Deliverable Number	D21.6	**Lead Beneficiary**	161 - Pfizer
Deliverable Name	Report on standard regulatory quality control parameters of mRNA formulations		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	50	**Work Package No**	WP21

Description
List of regulatory quality control parameters of LNP/EV (standard operating procedures for particles characterization, in vitro/vivo toxicology studies, benchmark materials)

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D21.7 – Regulatory compliant recommendations for rAAV analytics

Deliverable Number	D21.7	**Lead Beneficiary**	77 - KU Leuven
Deliverable Name	Regulatory compliant recommendations for rAAV analytics		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	58	**Work Package No**	WP21

Description
Validation of the currently available protocols for assessing the critical quality attributes of rAAV and develop new ones to increase accuracy and throughput

Deliverable D22.1 – Accelerator Hub inclusion criteria for research projects

Deliverable Number	D22.1	**Lead Beneficiary**	30 - AFM
Deliverable Name	Accelerator Hub inclusion criteria for research projects		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	12	**Work Package No**	WP22

Description
Description of criteria & process for identifying and selecting research projects for accelerator

Deliverable D22.2 – Impact analysis of Accelerator hub outputs 1

Deliverable Number	D22.2	**Lead Beneficiary**	22 - EATRIS
Deliverable Name	Impact analysis of Accelerator hub outputs 1		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP22

Description
Summary and assessment of support provided to projects

Deliverable D22.3 – Impact analysis of Accelerator hub outputs 2

Deliverable Number	D22.3	**Lead Beneficiary**	22 - EATRIS
Deliverable Name	Impact analysis of Accelerator hub outputs 2		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP22

Description
Summary and assessment of support provided to projects

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D23.1 – Best practice guidelines for creation and promotion of NMGs

Deliverable Number	D23.1	Lead Beneficiary	1 - INSERM
Deliverable Name	Best practice guidelines for creation and promotion of NMGs		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	6	Work Package No	WP23

Description
Guidance for countries to develop NMGs including information on successful implementation

Deliverable D23.2 – First report on the impact of NMGs

Deliverable Number	D23.2	Lead Beneficiary	170 - UNEW
Deliverable Name	First report on the impact of NMGs		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	36	Work Package No	WP23

Description
Analysis of the impact of the National Mirror Groups on ERDERA and on the national RD activities and strategies

Deliverable D23.3 – Second report on the impact of NMGs

Deliverable Number	D23.3	Lead Beneficiary	170 - UNEW
Deliverable Name	Second report on the impact of NMGs		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	80	Work Package No	WP23

Description
Analysis of the impact of the National Mirror Groups on ERDERA and on the national RD activities and strategies

Deliverable D23.4 – Recommendations on the NMG sustainability

Deliverable Number	D23.4	Lead Beneficiary	31 - CCUH
Deliverable Name	Recommendations on the NMG sustainability		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	77	Work Package No	WP23

Description
Recommendations how to maintain active and productive work of NMGs

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Deliverable D24.1 – Mapping of UCs specific needs and expectations 1

Deliverable Number	D24.1	**Lead Beneficiary**	27 - VULSK
Deliverable Name	Mapping of UCs specific needs and expectations 1		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	12	**Work Package No**	WP24

Description
Description of needs and expectations of underrepresented countries in ERDERA, including information on current barriers to participation

Deliverable D24.2 – Mapping of UCs specific needs and expectations 2

Deliverable Number	D24.2	**Lead Beneficiary**	27 - VULSK
Deliverable Name	Mapping of UCs specific needs and expectations 2		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	48	**Work Package No**	WP24

Description
Description of needs and expectations of underrepresented countries in ERDERA, including information on current barriers to participation

Deliverable D24.3 – Focused guidelines for actions at the National level 1

Deliverable Number	D24.3	**Lead Beneficiary**	93 - REUH
Deliverable Name	Focused guidelines for actions at the National level 1		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	24	**Work Package No**	WP24

Description
Development of focused guidelines for actions at the National level for capacity development of UC R&I

Deliverable D24.4 – Focused guidelines for actions at the National level 2

Deliverable Number	D24.4	**Lead Beneficiary**	93 - REUH
Deliverable Name	Focused guidelines for actions at the National level 2		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	48	**Work Package No**	WP24

Description
Development of focused guidelines for actions at the National level for capacity development of UC R&I

Deliverable D24.5 – Guidelines to increase UCs integration in ERDERA (including in funding activities) 1

Deliverable Number	D24.5	**Lead Beneficiary**	32 - AICIB
Deliverable Name	Guidelines to increase UCs integration in ERDERA (including in funding activities) 1		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	12	**Work Package No**	WP24

Description
Recommendations for procedures and measures to be implemented to increase UCs participation, including guidelines for promoting the inclusion of UCs in ERDERA funded actions (JTCs, Networking Calls, and others)

Deliverable D24.6 – Guidelines to increase UCs integration in ERDERA (including in funding activities) 2

Deliverable Number	D24.6	**Lead Beneficiary**	32 - AICIB
Deliverable Name	Guidelines to increase UCs integration in ERDERA (including in funding activities) 2		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	48	**Work Package No**	WP24

Description
Recommendations for procedures and measures to be implemented to increase UCs participation, including guidelines for promoting the inclusion of UCs in ERDERA funded actions (JTCs, Networking Calls, and others)

Deliverable D24.7 – Guidelines to increase UCs integration in ERDERA (including in funding activities) 3

Deliverable Number	D24.7	**Lead Beneficiary**	32 - AICIB
Deliverable Name	Guidelines to increase UCs integration in ERDERA (including in funding activities) 3		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	72	**Work Package No**	WP24

Description
Recommendations for procedures and measures to be implemented to increase UCs participation, including guidelines for promoting the inclusion of UCs in ERDERA funded actions (JTCs, Networking Calls, and others)

Deliverable D25.1 – White paper on ERNs Living Lab 1

Deliverable Number	D25.1	**Lead Beneficiary**	39 - ASU-FC
Deliverable Name	White paper on ERNs Living Lab 1		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP25

Description
White paper on the advancement and outputs of the 24 ERNs Living Lab

Deliverable D25.2 – White paper on ERNs Living Lab 2

Deliverable Number	D25.2	**Lead Beneficiary**	39 - ASU-FC
Deliverable Name	White paper on ERNs Living Lab 2		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP25

Description
White paper on the advancement and outputs of the 24 ERNs Living Lab

Deliverable D25.3 – Sustainability Plan for established strategic alliances and partnerships

Deliverable Number	D25.3	**Lead Beneficiary**	7 - ZonMw
Deliverable Name	Sustainability Plan for established strategic alliances and partnerships		
Type	DEM — Demonstrator, pilot, prototype	**Dissemination Level**	SEN - Sensitive
Due Date (month)	75	**Work Package No**	WP25

Description
Strategies for long-term collaboration as part of the overarching ERDERA exit strategy

Deliverable D25.4 – Publication on the International CRNs

Deliverable Number	D25.4	**Lead Beneficiary**	34 - RDI
Deliverable Name	Publication on the International CRNs		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	84	**Work Package No**	WP25

Description
White Paper on the International Dimension of the Clinical Research Networks

Deliverable D26.1 – OEI - Requirement No. 1

Deliverable Number	D26.1	**Lead Beneficiary**	1 - INSERM
Deliverable Name	OEI - Requirement No. 1		
Type	ETHICS	**Dissemination Level**	SEN - Sensitive
Due Date (month)	1	**Work Package No**	WP26

Description
Ethics Advisor_The proposal already provides for the appointment of an independent Ethics Advisor. Periodic reports by the Ethics Advisor must be submitted to the granting authority every 12 months, starting at M12 of the project. The CVs and declarations of absence of conflict of interest for the selected EA(s) must be kept on file and provided to the granting authority upon request. European Commission Guidance for Ethics Advisors/Boards can be found at: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/roles-andfunctions-of-ethics-advisory-ethics-advisory-boards-in-ec-funded-projects_he_en.pdf

Deliverable D26.2 – OEI - Requirement No. 2

Deliverable Number	D26.2	**Lead Beneficiary**	1 - INSERM
Deliverable Name	OEI - Requirement No. 2		
Type	ETHICS	**Dissemination Level**	SEN - Sensitive
Due Date (month)	12	**Work Package No**	WP26

Description
First report by the Ethics Adviser.

Deliverable D26.3 – OEI - Requirement No. 3

Deliverable Number	D26.3	**Lead Beneficiary**	1 - INSERM
Deliverable Name	OEI - Requirement No. 3		
Type	ETHICS	**Dissemination Level**	SEN - Sensitive
Due Date (month)	24	**Work Package No**	WP26

Description
The second report by the Ethics Adviser.

Deliverable D26.4 – OEI - Requirement No. 4

Deliverable Number	D26.4	**Lead Beneficiary**	1 - INSERM
Deliverable Name	OEI - Requirement No. 4		
Type	ETHICS	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP26

Description
The third report by the Ethics Adviser.

Deliverable D26.5 – OEI - Requirement No. 5

Deliverable Number	D26.5	**Lead Beneficiary**	1 - INSERM
Deliverable Name	OEI - Requirement No. 5		

Type	ETHICS	Dissemination Level	SEN - Sensitive
Due Date (month)	48	Work Package No	WP26

Description
The fourth report by the Ethics Adviser.

Deliverable D26.6 – OEI - Requirement No. 6

Deliverable Number	D26.6	Lead Beneficiary	1 - INSERM
Deliverable Name	OEI - Requirement No. 6		
Type	ETHICS	Dissemination Level	SEN - Sensitive
Due Date (month)	60	Work Package No	WP26

Description
The fifth report by the Ethics Adviser.

Deliverable D26.7 – OEI - Requirement No. 7

Deliverable Number	D26.7	Lead Beneficiary	1 - INSERM
Deliverable Name	OEI - Requirement No. 7		
Type	ETHICS	Dissemination Level	SEN - Sensitive
Due Date (month)	72	Work Package No	WP26

Description
Sixth report by the Ethics Advisor.

Deliverable D26.8 – OEI - Requirement No. 8

Deliverable Number	D26.8	Lead Beneficiary	1 - INSERM
Deliverable Name	OEI - Requirement No. 8		
Type	ETHICS	Dissemination Level	SEN - Sensitive
Due Date (month)	84	Work Package No	WP26

Description
Seventh report by the Ethics Advisor.

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LIST OF MILESTONES

Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
1	ERDERA Kick-off meeting	WP1	1 - INSERM	Minutes of the Kick-off meeting	1
2	Governance and Advisory Bodies set up	WP1	1 - INSERM	List of members	6
3	Number of funded Clinical trials with at least 50% of patients sample size recruited	WP4	5 - FTELE	Aggregated monitoring reports	80
4	Implementation of Networking Support Scheme	WP5	6 - LMT	Opening of funding scheme announced on ERDERA website	9
5	Establishment of Data Availability Committee (DAC)	WP6	8 - UT	Composition of DAC and report of first meeting	2
6	First federated data sharing and re-analysis approach focusing on genome data	WP6	8 - UT	First satellite instance (node) of the CRN Diagnostic Research	36
7	Long-read sequencing data included in data readiness processes for re-analysis	WP6	8 - UT	Updated process description and dataset identifier(s)	61
8	Establishment of Task Forces for Data Analysis (DATF) and interpretation (DITF)	WP6, WP7	10 - CNAG	Composition of DITF-DATF structure and report of first meeting	3
9	Phase I (yr 4-7): Data freeze for combined approach of distributed and federated analysis and interpretation, including non-standard approaches	WP7, WP6, WP15, WP8	10 - CNAG	Identifier of available Data sets for interpretation beyond standard exome and genome approaches	30
10	Phase II (yr 4-7): Data freeze for combined approach of distributed and federated analysis and interpretation, including non-standard approaches	WP7, WP6, WP15, WP8	10 - CNAG	Report on Data freeze including distributed/ federated access datasets to at least 10,000 data sets	48

Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
11	Phase I (yr 1-3): Data freeze for distributed analysis and interpretation	WP6, WP7, WP15	10 - CNAG	Report on 50,000 datasets analysed and interpreted through a distributed approach	36
12	Phase III: transition to federated approach completed	WP6, WP7, WP15, WP8	10 - CNAG	Demonstrator of Federated access to EU and non-EU partners of ERDERA	72
13	Analysis pipeline for long-read technologies established and tested on positive controls	WP8	11 - SRUMC	LRS-analysis pipelines tested, validated and released	36
14	New diagnoses of RDs by long-read technologies, RNA-DNA or multi-omics analyses established 1	WP8	11 - SRUMC	Report on Gene/loci identification by hidden variants utilizing innovative long-read methods and on Pathogenic variant identification by innovative data analysis	36
15	New diagnoses of RDs by long-read technologies, RNA-DNA or multi-omics analyses established 2	WP8	11 - SRUMC	Report on Gene/loci identification by hidden variants utilizing innovative long-read methods and on Pathogenic variant identification by innovative data analysis	84
16	DNA-RNA analysis pipelines established	WP8	11 - SRUMC	Pipelines tested, validated and released on selected repository for DNA-RNA analysis	60
17	Multi-omics analysis pipelines established	WP8	11 - SRUMC	Pipelines tested, validated and released on selected repository for multi-omics analysis	72
18	All institutional approvals for data extraction and sharing are in place	WP9, WP18	13 - UKHD	Confirmation of filing and provision on demand of the institutional approval documents	24
19	European and US databases interoperable for joint analysis	WP9, WP14	13 - UKHD	RDCA-DAP database in place	30
20	All integrated cohorts FAIRified and onboarded to VP	WP9, WP13, WP14	13 - UKHD	Cohorts queryable online	36
21	Proven interoperability of registries filled	WP9, WP14	13 - UKHD	Federated queries to participating registries operational	48

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Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
	automatically from different EHR systems in multiple countries				
22	Development and validation of disease-specific PROM scales 1	WP10	15 - VHIR	Core impact set for five demonstrator diseases published	18
23	Development and validation of disease-specific PROM scales 2	WP10	15 - VHIR	Core impact set for five demonstrator diseases published and corresponding PROM scale designed and corresponding PROM scale designed	24
24	Development and validation of disease-specific PROM scales 3	WP10	15 - VHIR	Core impact set for longitudinal validation in ≥ 3 languages completed	60
25	Development and revision of study protocols for the 4 use cases 1	WP10	15 - VHIR	Study protocols completed for the 4 use cases following standardised EC format	24
26	Development and revision of study protocols for the 4 use cases 2	WP10	15 - VHIR	Study protocols completed for the 4 use cases following standardised EC format and revised based on pilot studies	48
27	Anchoring of disease-specific indirect COAs to patient-relevant core impacts 1	WP10	15 - VHIR	Outcome matrix for indirect outcome assessments established	24
28	Anchoring of disease-specific indirect COAs to patient-relevant core impacts 2	WP10	15 - VHIR	Outcome matrix for indirect outcome assessments established and protocol for validation studies available; longitudinal anchoring studies completed for ≥ 2 COA assessments per use case	72
29	Anchoring of disease-specific indirect COAs to patient-relevant core impacts 3	WP10	15 - VHIR	Outcome matrix for indirect outcome assessments established and protocol for validation studies available; meaningful withinpatient change established	84

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Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
30	Standardized protocol for DALY and Cost of Illness	WP10	15 - VHIR	Document that details the standardized protocols for DALY and Cost of Illness are finalized	60
31	Target diseases ranking with at least 3 ranked diseases that matched to technology platforms	WP11	1 - INSERM	Report on a list of parameters indicating the selected diseases are qualified to be treated with technology platforms	24
32	List of ATMP dedicated Clinical Networks for the identified PoC platform	WP11	1 - INSERM	Listing of the networks and their clinical sites	24
33	Selection of the platforms best matched to prioritized target diseases	WP11	1 - INSERM	Identification of the best performing technological platform adapted to the treatment of the high-ranked diseases	36
34	Clinical Trial with ATMPs initiated	WP11	1 - INSERM	Clinical Trial Application filed	84
35	Preclinical efficacy studies use case 1 and 3 completed	WP12	16 - LUMC	Publication on results of efficacy studies	36
36	First patient treated in underrepresented country in a named patient setting	WP12	16 - LUMC	Pseudonymised Clinical Report	36
37	First patient treated in a named patient setting	WP12	16 - LUMC	Pseudonymised Clinical Report	48
38	Platform rolled out in 3 other centres	WP12	16 - LUMC	Clinical report and performance assessment report of platform roll-out	72
39	Landscape analysis of ERDERA data processing needs completed, including methodology for measuring acceleration rate of FAIRification	WP14	16 - LUMC	Report on analysis results and roadmap for addressing identified needs with risk mitigation measures	8
40	Data models and ingestion results validated against EOSC FAIR data publishing recommendations	WP14, WP13	16 - LUMC	Results of Automated compliance testing by the public FAIR Evaluator tool	36

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Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
41	First release of a portable data and analysis tracking system	WP6, WP7, WP16, WP14	19 - UMCG	Software available in GitHub	6
42	Initial version of the ERDERA analysis platform deployed	WP9, WP6, WP7, WP16, WP13, WP14, WP10	19 - UMCG	Platform available online	12
43	First version of the coordinated research diagnostics pipeline prioritised in 7 available for distributed implementation	WP9, WP7, WP16, WP10	19 - UMCG	Pipeline available in a public repository	24
44	Two use cases on federated analysis completed	WP15	19 - UMCG	Short report explaining the use cases outcomes, and the tools and services involved	36
45	First ontology versions for antenatal phenotypes for RD and functional impacts for RD	WP16	20 - AUMC	Demonstrator (involved Task 16.1; 16.2 and 16.5)	18
46	Treatabolome with crowd-sourcing functionality available	WP16	20 - AUMC	New version of the Treatabolome available online with the additional functionality (Task 16.3)	36
47	Graph-based infrastructure	WP16	20 - AUMC	A lightweight infrastructure to host, link to, and interlink semantic resources (Task 16.5)	80
48	Evaluation of the use of the Innovation Management Toolbox during within M1- M36 ERDERA lifespan	WP17	22 - EATRIS	Report delivered to the Executive and Governing Bodies	36
49	Composition of the Regulatory Support Group and first Kick off meeting	WP18	23 - FGB	Completion of composition and launch of Regulatory Support Group	3
50	First set of sources, guidance, recommendations and webinars delivered	WP18	23 - FGB	Documents and webinars available on project internal channels	20
51	Second set of sources, guidance, recommendations and webinars delivered	WP18	23 - FGB	Documents and webinars available on project internal channels	40

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Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
52	Regulatory recommendations for the technological deliverables of ERDERA	WP18	23 - FGB	Recommendations available on project internal channels	24
53	Interaction workflows with the Data Services and Acceleration Hub 1	WP19, WP16, WP21, WP22	24 - APHP	Report	36
54	Interaction workflows with the Data Services and Acceleration Hub 2	WP19, WP16, WP21, WP22	24 - APHP	Report	84
55	Yearly rounds of RD research education and training activities successfully delivered (Y1)	WP20	26 - EURORDIS	Datasets from satisfaction survey & participants acquired knowledge evaluation results	12
56	Yearly rounds of RD research education and training activities successfully delivered (Y2)	WP20	24 - APHP	Datasets from satisfaction survey & participants acquired knowledge evaluation results	24
57	Yearly rounds of RD research education and training activities successfully delivered (Y3)	WP20	26 - EURORDIS	Datasets from satisfaction survey & participants acquired knowledge evaluation results	36
58	Yearly rounds of RD research education and training activities successfully delivered (Y4)	WP20	26 - EURORDIS	Datasets from satisfaction survey & participants acquired knowledge evaluation results	48
59	Yearly rounds of RD research education and training activities successfully delivered (Y5)	WP20	26 - EURORDIS	Datasets from satisfaction survey & participants acquired knowledge evaluation results	60
60	Yearly rounds of RD research education and training activities successfully delivered (Y6)	WP20	26 - EURORDIS	Datasets from satisfaction survey & participants acquired knowledge evaluation results	72
61	Yearly rounds of RD research education and training activities successfully delivered (Y7)	WP20	26 - EURORDIS	Datasets from satisfaction survey & participants acquired knowledge evaluation results	84
62	Agreement on base manufacturing process of AAVs	WP21	28 - UC	Report/Plan	6
63	Immune cell lines available for mRNA technology platform	WP21	28 - UC	Delivery of specific primary T-cell lines and CAR-T cells as standard tools	12
64	Immune gene list content	WP21	28 - UC	Verification of the sequence of the genes	18

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Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
				applicable to the transcriptomic design for DD-PCR – data set	
65	Multiomics immune response analyses	WP21	28 - UC	Data set enabling selection of best suitable molecular, proteomics, metabolic, functional platforms, test for the further tasks of qualification and validation	24
66	Analytical toolbox for RNA formulations	WP21	28 - UC	Analytical toolbox for in vitro and in vivo characterization of efficiency, immunogenicity and safety of RNA formulations	36
67	Adoption of base manufacturing protocol and scale up	WP21	28 - UC	Report/Plan	36
68	Treg development candidate	WP21	28 - UC	Laboratory Cas-specific Treg prototype generated under non-GMP conditions available for in depth PoC preclinical studies	36
69	AAV production process scale up	WP21	28 - UC	Larger scale bioprocessing using bioreactors and suspension producer cells	36
70	Analysis and test of RNA sequences	WP21	28 - UC	Design, production, analytical characterization of RNA molecules, and head-to-head comparison of RNA sequences in reporter cell lines	42
71	Validation of the assays for selected CQAs (minimum being genome titer) with accompanying inter-laboratory variability analysis	WP21	28 - UC	Report	48
72	Identification of effective and safe gene delivery modalities for the selected organs	WP21	28 - UC	Validation across different Tasks	48
73	Selection of in vivo gene delivery modalities	WP21	28 - UC	In vivo ranking of gene delivery modalities for the selected organs	48

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Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
74	PoC of gene correction in relevant in vivo models of the selected diseases	WP21	28 - UC	Validation across different organs and diseases	58
75	Public-Private Partnership accelerator workflows completed	WP22	29 - FFRD	Set of SOPs	12
76	Public-Private Partnership accelerator marketplace construction completed	WP22	29 - FFRD	Webpages and inaugural meeting of investor launching accelerator	24
77	75% (23 out of 31) of NMGs established in ERDERA participating countries	WP23	1 - INSERM	Aggregated report including lists of participants and three-year plan of NMGs	12
78	100% of NMGs established in ERDERA participating countries	WP23	1 - INSERM	Aggregated report including lists of participants and three-year plan of NMGs	24
79	Successful gain and dissemination of specific knowledge among NMGs trough train the trainees and thematic workshops	WP23	1 - INSERM	Results of Annual NMG surveys on knowledge dissemination among local NMG members	84
80	Workshops on actions to improve UCs participation (back-to-back with funders meeting) 1	WP24	32 - AICIB	Reports including Statistical analysis of indicators implementation (number of actions implemented, number of actions accepted to implementation, etc.) to improve UCs participation in RDP funded activities	11
81	Workshops on actions to improve UCs participation (back-to-back with funders meeting) 2	WP24	32 - AICIB	Reports including Statistical analysis of indicators implementation (number of actions implemented, number of actions accepted to implementation, etc.) to improve UCs participation in RDP funded activities	48
82	Impact of UCs on ERDERA activities demonstrated 1	WP6, WP7, WP16, WP11, WP4, WP5, WP15, WP18, WP14, WP26,	32 - AICIB	Report Statistics analysis of implementation indicators (number of UCs cases describing impacts, number of UCs integrated in ERDERA activities)	48

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Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
		WP10, WP1, WP2, WP25, WP8, WP9, WP19, WP17, WP21, WP12, WP23, WP22, WP13, WP20, WP3, WP24			
83	Impact of UCs on ERDERA activities demonstrated 2	WP6, WP7, WP16, WP11, WP4, WP5, WP15, WP18, WP14, WP26, WP10, WP1, WP2, WP25, WP8, WP9, WP19, WP17, WP21, WP12, WP23, WP22, WP13, WP20, WP3, WP24	32 - AICIB	Report Statistics analysis of implementation indicators (number of UCs cases describing impacts, number of UCs integrated in ERDERA activities)	72
84	Two Task Forces (TF) per year completed (Y2)	WP25	7 - ZonMw	Article, white paper or planned outcomes of the Task Force	24
85	Two Task Forces (TF) per year completed (Y3)	WP25	7 - ZonMw	Article, white paper or planned outcomes of the Task Force	36
86	Two Task Forces (TF) per year completed (Y4)	WP25	7 - ZonMw	Article, white paper or planned outcomes of the Task Force	48
87	Two Task Forces (TF) per year completd (Y5)	WP25	7 - ZonMw	Article, white paper or planned outcomes of the Task Force	60
88	Two Task Forces (TF) per year completed (Y6)	WP25	7 - ZonMw	Article, white paper or planned outcomes of the Task Force	72

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Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
89	Two Task Forces (TF) per year completed (Y7)	WP25	7 - ZonMw	Article, white paper or planned outcomes of the Task Force	84
90	Three International Conferences organised	WP25	7 - ZonMw	Dates, programmes and reports of Conference on website	84

LIST OF CRITICAL RISKS

Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
1	Incapacity or departure of coordinator [(i) likelihood: Low, (ii) severity: High]	WP1	High quality of the coordination team with possibility of interim by one of the Workstream leaders. Strong commitment of the Coordinator.
2	Misuse of resources [(i) likelihood: Low, (ii) severity: High]	WP1	Most partners' institutions are experiences and equipped with internal financial accounting and auditing office. Close Data-Driven Monitoring will help in identifying abnormalities.
3	Financial bottleneck due to underestimation of contribution capacity of partner(s) and/or withdrawal of major partner [(i) likelihood: Medium, (ii) severity: High]	WP1	Detailed business plan prepared before launch of the project including 15% risk of budget loss. Financial management issues set up in Consortium Agreement. Emergency mitigation procedure set up – possibility to adjust the work plan and align budget-
4	Situations of force majeure [(i) likelihood: Medium, (ii) severity: Medium]	WP1	Agile management adapting to unforeseen events. Leveraging on past COVID-19 and Ukraine war experience (e.g., continuous information back-up on remote secured servers, hybrid/online shift of activities, strategic context intelligence).

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Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
5	Insufficient coordination of priorities / unresolved conflicts about strategy [(i) likelihood: Low, (ii) severity: Medium]	WP1	Criteria and process of prioritization agreed at the start of the project and validated by GB; Possibility to call for MAB recommendations; Flexibility of Annual Work Plans.
6	National financial bottlenecks for funding joint transnational research projects [(i) likelihood: Medium, (ii) severity: Medium]	WP3	Earmarking adequate national budgets in line with national research capacity and costs; Postevaluation negotiations on increasing national budget and/or budget negotiations with applicants; Use of EC co-funding to adjust national budget shortcomings.
7	Delay in the clinical trials progress (e.g., difficulties in recruiting subjects; difficulties in obtaining approvals by competent authorities) [(i) likelihood: Medium, (ii) severity: Medium]	WP4	The second step pf evaluation focuses on feasibility such that funded trials should be ready for approval. Active involvement of PAOs in the CTs. Payments against achievements of the milestones.
8	Delay in implementation and scalation of federated diagnostic research approach [(i) likelihood: High, (ii) severity: Medium]	WP6, WP7, WP15	Focus on National 1+MG/GDI infrastructures that are ready such as France and Sweden first, then progress according to readiness status.
9	Delay in data availability and sharing [(i) likelihood: High, (ii) severity: Medium]	WP6	According to data availability status, the sharing of data will be phased. While the risk for some centres for delay is high, the overall risk is medium or lower since delivering centres will compensate for delayed ones.
10	Delay in or Slower distributed re-analysis of REAL datasets [(i) likelihood: Medium, (ii) severity: Medium]	WP6, WP7, WP15	Apply to use EuroHPC resources. Include additional local clusters for the analysis. Prioritise reanalyses with higher solve rate. Phasing of re-analysis according to readiness levels.
11	Long-read technologies (and analyses) do not progress as fast as anticipated [(i) likelihood: Medium, (ii) severity: Medium]	WP7, WP8	Less recent (and/or contributed) data available than estimated, enlarge focus on re-analysis of already available data (6/7). Purposely, long-read data processing is based on three technologies to mitigate risk and adapt (PacBio, ONT, Bionano).
12	Too few (matched) DNA-RNA (or other -omics) datasets provided by partners [(i) likelihood: Medium, (ii) severity: Medium]	WP8	Integrative tools can largely be employed on already available data (e.g., Solve-RD); select best available use cases from new data. Data and tool federation (by 6-8) will allow including more data.
13	EHR access and linkage between registries and social security data restricted by local regulations	WP9	Good feasibility of initially selected use-cases; enrolment of alternative ERDERA partners to project; seek support from regulators & interaction with the EHDS.

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Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
	and difficult to generalize across Europe [(i) likelihood: Medium, (ii) severity: High]		
14	Data content and/or quality of patient cohorts insufficient [(i) likelihood: Low, (ii) severity: High]	WP9	Quality check of dataset extracts and metadata for cohort selection, review of existing pilot studies using selected cohorts, data improvement measures from DSH for still active cohort studies.
15	Insufficient predictive power of disease progression models [(i) likelihood: Low, (ii) severity: High]	WP9	Modify analytical approaches, obtain more / better data by international collaborations.
16	Delay in Outcome Research validation studies at some clinical site [(i) likelihood: Medium, (ii) severity: High]	WP10	Expand the network of study sites by additional ERN sites to ensure rapid recruitment.
17	PROMs not sensitive to change in the timeframe of validation studies (2 years) [(i) likelihood: Medium, (ii) severity: High]	WP10	Highly sensitive indirect COAs will be included and anchored to patient-relevant core impacts.
18	Delays on outcome research clinical studies implementation due to regulatory or ethics issues [(i) likelihood: Medium, (ii) severity: High]	WP10	Feasibility assessment of clinical sites. Early initiation of regulatory and ethics clearance tasks. Build on successful cross border cases of implementation of mHealth.
19	Patients not adhering to the clinical protocol [(i) likelihood: Low, (ii) severity: High]	WP10	Patient Engagement workshops in collaboration with EURORDIS, ePAGs and National Pos. Clinical protocol co-designed with patients.
20	No positive results from the PoC studies [(i) likelihood: Medium, (ii) severity: High]	WP11	Leverage on the experience from the high number of highly promising results obtained using various ATMPs platforms in preclinical models.
21	Difficult to implement ASO platform beyond initial partners, especially in centres from underrepresented countries [(i) likelihood: Medium, (ii) severity: Medium]	WP12	Not all components have to be implemented locally, treatment board, ASO design and testing can be done at LUMC and UT. Proactive support from ERNs for the individualised part of platform implementation.
22	New resources require significant modifications on the design and implementation of the RD-VP and its components, beyond the capacity of	WP13	RD-VP flexibility and design, with minimal requirements for onboarding resources.

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Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
	the allocated resources [(i) likelihood: Low, (ii) severity: Medium]		
23	Resources experiencing legal or IPR barriers to onboard [(i) likelihood: Medium, (ii) severity: Medium]	WP13	Legal, regulatory and IPR support from ERDERA experts to de-risk onboarding process.
24	CRN and funded projects deploy insufficient resources to contribute to the ERDERA-Data Hub [(i) likelihood: High, (ii) severity: Medium]	WP12	Earmarked CRN and JTC grant funding contributing to EREDERA Data Hub (ii) Added value demonstrated for the first projects contributing to the Data Hub.
25	Complexity of data and data access is greater than expected, or inability to address on-time the demand [(i) likelihood: High, (ii) severity: Medium]	WP14	Feasibility assessment of the request to DSH including flexible data processing scenarios. FAIRification targets will be reprioritized to ensure a critical mass is reached for analysis. Methodology can be developed based on historical data, as well as on simulated data addressingEthical and Regulatory related issues.
26	Data and analysis system not meeting the CRN needs [(i) likelihood: Low, (ii) severity: Medium]	WP15, WP14	Revise AGILE methodology with short-term sprints and promote higher involvement of end users in the process.
27	Insufficient compute and/or storage capacity available for the CRN and funded project needs [(i) likelihood: Medium, (ii) severity: Medium]	WP9, WP6, WP7, WP15, WP14, WP10, WP8	Collaboration with EU compute and storage initiatives (already initiated). Limit processing to downstream data (e.g. VCF files) and exclude raw data from analysis (e.g. full sequences). Prioritise focused analyses (e.g., on particular patient groups).
28	Insufficient resources to code portable pipelines and support local implementations for diagnostics. [(i) likelihood: Low, (ii) severity: Medium]	WP7, WP15, WP8	Leverage existing open-source pipelines. Rely on locally implemented pipelines (even if not portable versions).
29	GDI infrastructure and/or GA4GH standards not fit for purpose on time for federated learning [(i) likelihood: Medium, (ii) severity: Medium]	WP6, WP7, WP15, WP14	Bring in alternative solutions developed and/or implemented by participating partners in other projects (e.g. Genomed4All, DataSHIELD).
30	Fail to collaborate with HPO to extend its content to prenatal echographic phenotypes [(i) likelihood: Low, (ii) severity: Medium]	WP16	Collaborative generation of a stand-alone ontology of prenatal phenotypes of RD and an ontological module in ORDO.

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Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
31	Difficulty engaging with experts and patient organisations annotating RD with functional consequences [(i) likelihood: Medium, (ii) severity: Medium]	WP16	Revise prioritization of RD based on opportunities for collaboration after specific dissemination efforts to engage with stakeholders.
32	Low engagement of experts [(i) likelihood: Low, (ii) severity: High]	WP17, WP18	Leverage on existing database of already committed experts. Training and engagement activities. Recognition of the expert support to projects funded by ERDERA.
33	Low awareness of the services provided [(i) likelihood: Low, (ii) severity: Medium]	WP17, WP18	Maximizing the dissemination of the services by the communication & Dissemination task and by ERDERA Partner.
34	Non-availability of education and training providers for emerging training needs [(i) likelihood: Medium, (ii) severity: Medium]	WP20	Recruitment of training providers from ERDERA partners, extended to national systems (through NMGs) and to collaboration with other initiatives.
35	Insufficient number of education and training participants [(i) likelihood: Low, (ii) severity: Medium]	WP20	Increased awareness-raising and dissemination efforts in collaboration with 2, targeted at national systems (through NMGs) and RD research ecosystem (through ERDERA partners and collaborations).
36	In Vitro Transcription Amplification of DNA or RNA fails [(i) likelihood: Low, (ii) severity: Medium]	WP21	Development of recombinant production in yeast (ART-ARNm)
37	Therapy response and immunogenicity evaluation hampered by poor efficacy and/or delays in the technology development of T21.1 - T21.4 [(i) likelihood: Low, (ii) severity: Medium]	WP21	Application of relevant "use cases" (i.e., known gene therapy tools) to develop the test platforms in T21.5)
38	Low frequency of antigen-specific B cells in peripheral blood limiting the detection and/or selection and expansion of specific B cells [(i) likelihood: Medium, (ii) severity: Medium]	WP21	Samples from patients with preformed immunity or vaccinated as model systems to establish the B-cell methods.
39	There are not enough projects with high potential	WP22	Initial ERDERA strategy fostering preclinical development as potential target for the calls

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Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
	for acceleration, resources to bring projects to investment-readiness, and interest from investors. [(i) likelihood: Low, (ii) severity: High]		& matching the strategy of interested investors. Opening the accelerator services to external funding organisations/ initiatives with interest in RDs.
40	NMG not implemented in all EU participating countries after the second year of ERDERA [(i) likelihood: High, (ii) severity: Medium]	WP23	Potential NMGs already identified in 15 (out of 31) EU countries. Dissemination of the added value of existing NMGs (established in EJP RD). Close collaboration with national stakeholders.
41	Inactive or non-compliance of NMGs with the foreseen activities [(i) likelihood: Medium, (ii) severity: Medium]	WP23	Close monitoring of NMG activities and Financial support provided to active ones.
42	Potential lack of commitment by underrepresented countries and/or modifications in national priorities/ national contact points (due to governmental shifts) [(i) likelihood: Medium, (ii) severity: Medium]	WP24	Involvement, by design, of national representatives (policy makers, academics, clinicians, patient representatives, industry) and good communication with the national stakeholders.

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PROJECT REVIEWS

Project Reviews

Grant Preparation (Reviews screen) — Enter the info.

Review No	Timing (month)	Location	Comments
RV1	12	online	5 experts
RV2	24	online	5 experts
RV3	36	online	5 experts
RV4	48	online	5 experts
RV5	60	online	5 experts
RV6	72	online	5 experts
RV7	84	online	5 experts

Part B: technical description

ERDERA - EUROPEAN RARE DISEASES RESEARCH ALLIANCE

[This document is tagged. Do not delete the tags; they are needed for processing.] #@APP-FORM-HECOFUND@#

HISTORY OF CHANGES

Version (date)	Changes	Page
	Annex 1 Part A	
29.02.2024	Correction of the ISO code for Portugal (from PO to PT) and Poland (from PO to PL)	NA
	Change of Beneficiaries acronyms (from Utartu to UTARTU; from ICS to VHIR; from AMC to AUMC; from Uhasselt to UHASSELT; from AOU MEYER IRCCS to AOU Meyer IRCCS; from Centogene AG to Centogene; from Copenhagen Economics to CE; from REGIONH (Copenhagen University Hospital) to REGIONH; from FHG to Fraunhofer; from RS (GMS-GMCK) to RS; from MAPI Research Trust to MRT; from SCIENSANO to Sciensano; from SONIO to Sonio; from University of Campania L. to UNICAMPANIA; from University of Crete to UoC; from Cadi Ayyad University to CAU; from Aalborg University Hospital to Aalborg UH; from Aarhus Univeristy Hospital to Aarhus UH; from IABS to IABS-EU; ; from CRG to CRG-CERCA; from GMS-Skane Region to GMS-RS.	NA
	Removal of Beneficiaries: 59-Fraunhofer UK; 62-GA UK; 85-UNEW; 86-CUH; 90-PMU; 128-ULEIC;143-QUB-UK; 149-UCL; 151-UCAM.	NA
	Addition of Beneficiaries: 59-IFD; 62-MZd; 85-MoH SR; 86-RDG; 90-JSI; 128-UANTWERPEN; 148-IPG; 149-UO.	NA
	Addition of Affiliated Entities to Beneficiaries: 60-FSJD-CERCA – 60.1-HSJD; 62-MZd – 62.1-AZV; 136.-LMU – 136.1-KUM.	NA
	Addition of Associated Partners: 167*-Fraunhofer UK; 168*-GA UK; 169*-UNEW; 170*-CUH; 171*-ULEIC; 172*-QUB-UK; 173*-UCL; 174*-UCAM.	NA
	Removal of Associated Partners: 170*-Utrecht UMC; 171*-LH (LabCorp).	NA
	Addition of Deliverables: D1.14 Report on cumulative expenditure incurred (M12); D1.7 Annual Work Plan 6 (M69); D2.1 Project website (M3).	NA
	Removal of Deliverables: D1.13 Annual Progress Report 6 (M75).	NA
	Modification of Deliverables due date: D1.8 from M15 to M18; D1.9 from M27 to M36; D1.10 from M39 to M54; D1.11 from M51 to M72; D1.12 from M63 to M84.	NA
	Change of Deliverables Lead Beneficiary: D13.1, D13.2, D13.3 from Utwente/INSERM to INSERM; D14.1, D14.2, D14.3 from AMUC/SRUMC/LUMC to LUMC; D22.2, D22.3 from EATRIS/FFRD to EATRIS; D24.1, D24.2 from VULSK, REUH to VULSK; D24.3, D24.4 from REUH, VULSK to REUH; D24.5, D24.6, D24.7 from AICIB, IMGGE to AICIB; D25.1, D25.2 from ASU-FC, HSJD to ASU-FC.	NA
	Removal of Milestones: MS2.1 Initial set of tools and activities (M6).	NA
	Precision in WP 1 description for the task 1.3 “Monitoring of the Partnership activities” that this task will also consider criteria on ERDERA Results exploitability by non-rare conditions; application of these criteria to funded research activities will be considered in the funding opportunities. This addresses the recommendation provided through the proposal reviewers’ feedback.	NA

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	Change of PIC from 998732274 to 919322739 for 28-AUMC; from 882251279 to 939076692 for 59-IFD; from 880953613 to 999602073 for 87-REGIONSYD; from 884513125 to 997381064 for 130-AalborgUH; and from 904861591 to 999977172 for 174-UCAM	NA
20.03.2024	Addition of Deliverables: D1.14 Report on cumulative expenditure incurred (M12)	NA
	The deliverable "Annual Progress Report 1" has the delivery date been shifted from Month 18 to Month 24	NA
	Removal of Beneficiary 137. LUni	NA
	Addition of Affiliated Entities to Beneficiaries: 1. INSERM – 1.1 CAD.	NA
	Change of PIC from 944342531 to 878333449 for 43-CENTOGENE	NA
30.04.2024	Harmonisation of Beneficiaries acronyms from ISCIII-IIIER/ISCIII-SGIPRI to ISCIII; from CUH (NIHR-RDBR) to CUH; from UTartu to UTARTU; from ICS/ and ICS/VHIR to VHIR; from Astra Zeneca to AZ; from AMC or AMUC to AUMC; from Uhasselt to UHASSELT; from Centogene to CENTOGENE; from Copenhagen Economics to CE; from RS (GMS-GMCK) to RS; from MAPI Research Trust to MRT; from SCI to Sciensano; from GMS-Skane Region to GMS-RS; from Otago University to UO; from NIHDRJ to INSA; from Rare Care Centre to RCC; from Sorbonne University to SU; from Motol University to MUH; from GFGGRD to GERAD	NA
	Update of the Task 1.3 description to address the reviewers shortcoming and recommendation on the under-represented countries involvement.	NA
	Update of Task 1.1 to address the reviewers recommendation on synergy with the EU Cancer Mission and the EU Beating Cancer Plan	NA
	Update of Task 1.4 to address the reviewers recommendation, from the sustainability perspective, on the high-level, open, interactive, systematic, and appropriately resourced process to co-create the articulation of problems and solutions that make best use of available resources.	NA
	Removal of Affiliated entity "60.1- HSJD" and integration as beneficiary "150 - HSJD"	NA
	Addition of the beneficiary "MSW" that was missing in the task 1.3 "Monitoring of the Partnership activities"	NA
	Addition of the beneficiary "NKUA" that was missing in the contributing organisation list of task 6.2. "Data standardisation, sharing, and federation" and task 6.3 "Data access and returning research results"	NA
	Addition of the beneficiary "CRG-CERCA" that was missing in the contributing organisation list of task 14.2 "Data ingestion tools"	NA
	Harmonisation of the acronym of the following organisations listed in the task 25.3 "Promote the International Dimension of the CRN of ERDERA by building global networks among CRNs and patient organizations": from "CHEO-RI*(Care4Rare NMD4C)" to "CHEO-RI*); from "Rare Care Centre*" to "RCC*".	NA
	WP23 description updated within the section "Objectives" with one last sentence to further address the proposal reviewers recommendation on the link with ongoing initiatives and structures under the EU Cancer Mission and EU Beating Cancer Plan.	NA
	Addition of VHIR as contributing beneficiary to tasks 17.1. "Execution of the Mentoring Program" and 17.2 "Consultancy service"	NA
30.05.2024	Harmonisation of Beneficiaries acronyms from Fraunhofer to FHG and from UPPMD to WDO	NA
	Removal of 114 UKA from WP20 task	NA

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	Update of Person-months table in WP2, WP20, WP23	NA
	Update of the names of the Deliverables D1.8, D1.9, D1.10, D1.11 and D1.12 from "Annual Progress Report" to "Periodic Progress Report"	NA
	Completion of the list of organisation mentioned as contributors next to the tasks 6.1, 6.2 and 6.3 to precisely show all the involved organisations.	NA
	Update of the list of the organisations involved in tasks 9.1, 9.4 and 10.1 by adding the organisation "KUM" (the affiliated entity of the beneficiary "LMU")	NA
	Completion of the list of organisation mentioned as contributors next to the tasks 3.1 and 3.2 to precisely show all the involved organisations.	NA
18.06.2024	Update of the due dates (in Months) of the Periodic Progress Reports as per the EC recommendation (D1.8, D1.9, D1.10, D1.11 and D1.12 updated to M26, M44, M62, M74 and M84 respectively)	NA
	Correction of the organisations list leading the task 21.1 by re-introducing 63-GNT as co-leader	NA
	Correction of the organisations list leading the task 21.2 by re-introducing 55-FHG as co-leader	NA
	Correction of the organisations list leading the task 21.2 by re-introducing 124-CNRS as co-leader	NA
	Addition of 70-IMAGINE to the list of the organisations leading the task 21.4	NA
	Update of the organisations list contributing to task 11.4	NA
	Annex 1 Part B	
29.02.2024	Addition of the table of content	5
	Addition of List of Abbreviations	7
	"Heading 3" numbering of the section "1.1 Objectives and ambition of the Partnership"	13, 14, 15, 16
	"Heading 3" numbering of the section "1.2 Methodology"	18,19, 24, 25, 26
	"Heading3" numbering of the section "2.1 Project's pathways towards impact"	26, 27, 28, 29, 30
	"Heading 3" numbering of the section "2.2 Measures to maximise impact"	34, 36
	Table 3.1h, update of the partners' number: from 54-FTELE to 5-FTELE;	41
	Table 3.1h, update of partner from: 15-ICS to 15-VHIR	41
	Table 3.1h: 'Purchase costs' items update: beneficiary 22- EATRIS increase of amount justified, change from 15-ICS to 15-VHIR and change from 136-LUM to 136.1-KUM)	41
	Table 3.1i, update of the partners' number: from 147-Vinnova to 144-Vinnova; from 15-CIHR* to 152-CIHR*; from 156-DFG* to 153-DFG*; from 158-FRQS* to 155-FRQS*; from 168-SNSF* to 165-SNSF*	43
	Table 3.1i: 'Other costs categories' items (e.g. internally invoiced goods and services) update: addition of new beneficiaries' budget: 59-IFD and 62-MzD, decrease of budget beneficiary 7-ZonMw	43
	Table 3.1j addition of the third party providing 'In-kind contributions "Protisvalor Mediterranée SAS (PVM)" for the beneficiary 37-AMU	44
	"Heading 3" numbering of the section "3.2 Capacity of participants and consortium as a whole"	45
	Addition of section "4. Ethics self-assessment" including the ethics self-assessment submitted in the proposal Part A and the result of the Ethics Screening Report.	49
	Deleted from the header the following reference text: "Call: HORIZON-HLTH-2023-DISEASE-07-01:European Partnership on Rare Diseases" and "EU Grants: Application form (HE Cofund): V3.1 -08.09.2022"	NA
	Updated the footer as follow ""[Proposal number] – [Proposal acronym] – Part B – [Page number (starting at 1 for Part B)]"	NA
	Tables 3.1a, 3.1b, 3.1c, 3.1d, 3.1e and 3.1f removed from section 3.1. Their information is included in Part A.	NA

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

20.03.2024	Addition of a Paragraph with references at the end of the section "1.1.1 Europe's journey and commitment to Rare Diseases" and to further support the "vision and mission" of ERDERA, addressing thus the proposal reviewers' feedback on the "excellence criterion".	13
	Precision in the section "1.2.5 Data Management Plan" that the Data Management Plan will be constantly updated, and the resulting version will be submitted at each reporting period to comply with the European Commission request for precision.	24
	Section "2. Impact" updated to accommodate the Sustainable Development Goals inclusion and their linkage with respective ERDERA activities and targets.	26, 29, 30
	Modification of the cells "mitigation measures" in the table Impact for the Expected outcome 1 and the expected outcome 2, further clarifying how potential negative impacts are mitigated, and addressing the proposal reviewers' feedback on the impact criterion.	27
	Figure 4 added to show the synergies and integrations between work packages.	40
	Update of Table 3.1h: 'Purchase costs	41
	Addition of paragraphs in the section "3.2.1. Governance", adding details regarding the decision-making process, the links to the Strategic Research and Innovation Agenda and the annual workplans, drawing from what is described in the AWPY1, addressing thus the proposal reviewers' feedback on the "implementation" criterion.	47
30.04.2024	Update of Table 3.1g: 'Subcontracting costs' items, items following request of EC.	49
	Update of Table 3.1h: Purchase costs items following request of EC.	49
	Update of Table 3.1i: 'Other costs categories' items following request of EC.	62
	The Governance section was updated according to the suggestions provided by DG RTD.	66-69
30.05.2024	Harmonisation of Beneficiary acronym from UPPMD to WDO	71
	Update of Table 3.1h: 'Purchase costs'	56, 57, 61, 64, 635
	Update of the section 4.1 "The Ethics Screening Report" with the additional Ethics Requirements	83-86
18.06.2024	Update of Table 3.1h based on EC comments	53, 54, 55, 56, 57, 58, 62, 64
	AWP Y1	**Page number of AWP Y1 document**
29.02.2024	WP2: addition of a sentence to add the D2.1 "Project website" in the description of the text	31
	New Beneficiary 59-IFD has been added	34, 158
	New Beneficiary 62-MZd has been added	34, 159
	The affiliated entity 62.1 - AZV has been added	34, 159
	Beneficiary 145-Vejle hospital has been merged with Beneficiary 87-REGIONSYD	43, 167, 168
	New Beneficiary 149-UO has been added	44, 46, 47, 124, 125, 127, 185
	New Beneficiary 128-UANTWERPEN has been added	44, 46, 47, 178
	New Beneficiary 148-IPG has been added	44, 46, 47, 184
	Addition of the partner 84-NKUA as contributor in the tasks 6.2 and 6.3	46, 47

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	The affiliated entity 136.1 - KUM has been added	57, 242
	Beneficiary 59-Fraunhofer UK has been switched to Associated Partner 167*-Fraunhofer UK	58, 189, 190
	Beneficiary 62-GA UK has been switched to Associated partner 168*-GA UK	58, 190
	Partner 55-FHG has been removed of the contributors of the WP11 (General table of WP11 and Task 11.3	66, 67
	Change on the WP13 lead: from UTWENTE/LUMC to INSERM (WP & deliverables): changes in the 1st table and in the task 13.1 and in the table 2.3.b "AWP set of activities" and in the description of the partners	84, 155
	Associated Partner LH has been removed	93, 95, 109, 113, 114, 190
	Beneficiary 90-PMU has been removed and replaced by Beneficiary 141-PLUS in the impacted tasks	97, 98, 99, 168
	Affiliated entity Fraunhofer IBMT has been deleted	100, 106, 193
	Beneficiary 15-ICS has been replaced with 15-VHIR	112, 144, 152, 209
	Contributor 140-PEI has been replaced by 55-FHG in task T21.3.6	116
	New Beneficiary 85-MoH SR has been added	123, 124, 125, 127, 166, 167
	New Beneficiary 86-RDG has been added	123, 124, 125, 127, 166, 167
	New Beneficiary 90-JSI has been added	124, 125, 127, 168
	Addition of new National Mirror Groups to be developed in the Y1 and later in the WP23	125
	Beneficiary 13-UKHD partner's description of "Expertise, available infrastructure(s)" has been updated to reflect the involvement of all the research teams	143
	Addition in the partner description of partner 37-AMU of a text precising that AMU will have their administrative tasks performed by a spin off company	152
	Mention of the Gender equality plan of the partner 65-Region Stockholm in the admin form and in the AWP Y1	160
	Beneficiary 86-CUH has been switched to Associated partner 170*-CUH	166, 190
	Beneficiary 85-UNEW has been switched to Associated Partner 169*-UNEW	166, 190
	Beneficiary 128-ULEIC has been switched to Associated Partner 171*-ULEIC	177, 190
	Beneficiary 143-QUB-UK has been switched to Associated Partner 172*-QUB-UK	180, 190
	Beneficiary 149-UCL has been switched to Associated Partner 173*-UCL	180, 190
	Beneficiary 151-UCAM has been switched to Associated Partner 174*-UCAM	182, 190
	Associated Partner Utrecht UMC has been removed	190, 199
	Partner numbers from 137 to 174 have been changed	NA
	Change of Beneficiaries acronyms (from Utartu to UTARTU; from I; from AMC to AUMC; from Uhasselt to UHASSELT; from AOU MEYER IRCCS to AOU Meyer IRCCS; from Centogene AG to Centogene; from Copenhagen Economics to CE; from REGIONH (Copenhagen University Hospital) to REGIONH; from FHG to Fraunhofer; from RS (GMS-GMCK) to RS; from MAPI Research Trust to MRT; from SCIENSANO to Sciensano; from SONIO to Sonio; from University of Campania L. to UNICAMPANIA; from University of Crete to UoC; from Cadi Ayyad University to CAU; from Aalborg University Hospital to Aalborg UH; from Aarhus Univeristy Hospital to Aarhus UH; from IABS to IABS-EU; ; from CRG to CRG-CERCA; from GMS-Skane Region to GMS-RS; from Roche (Spartx) to ROCHE, from FDB (Fujifilm) to FDB, from NIHDRJ to INSA, from GFGGRD to GERAD, From INSERM_CAD to CAD	NA
20.03.2024	Addition of a sentence regarding resource allocation was added in the monitoring task in the WP1 on the AWP Y1.	26
	Addition of a reference regarding the work on strategy and alignment aspects in EJP RD	241

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	Update of tables Table 2.3.d: Summary of staff effort for Year 1, Table 2.3.d - Bis: Summary of staff effort for the three years, Table 2.3.e: 'Purchase costs' items for the three years and for Year 1	NA
	Removal of duplicated tables in Annual Work Plan Year 1: Table 3.1g: 'Subcontracting costs' items, Table 3.1i: 'Other costs categories' items (e.g. internally invoiced goods and services), Table 3.1j: 'In-kind contributions' provided by third parties	NA
	Removal of a beneficiary: 137-Luni	NA
30.04.2024	Removal of the following organisations from the Person-Month table of WP1 to comply with the budget distribution for Year 1: ELS (52); FFRD (29); FTELE (5); ISCIII (72); LMT (6)	17
	Addition of the mention 'Beneficiaries providing in-kind contribution' in the efforts table (Person-Months table) in the WP1, WP3 and WP11 description.	17, 36, 73
	WP1, **T1.2. Governance & strategy,** The following sentence was revised to underline widening measures. "The strategic process will involve additionally the MAB and the National Alignment Board, the latter being specifically important for the implementation of measures related to the active participation of countries and widening measures". The following sentence was revised to underline widening measures.	22
	Removal from the WP2 "Person Months" table the beneficiaries with no budget in WP2 (i.e., INSERM, EURORDIS, UPPMD, FFRD, TEDDY) as they will be contributing to these activities within their other work packages.	30
	Harmonisation of Beneficiary acronym from Tuscreg to RT(Tuscreg)	36
	The duplication of the 'ISCIII' organization in the listing of the contributors of task 3.1, 'Call topic selection for JTCs and Clinical Trials' has been removed.	38
	Revision of a sentence in the ST3.2.1. "Preparation of the first joint transnational call and establishment of the joint call secretariat", underlining the "widening measures", to the proposal reviewers feedback on the involvement of widening countries.	39
	Correction of the numbering of the subtask "Ethics evaluation of projects recommended for funding of the first joint transnational call" from "ST3.2.3.1" to "ST3.2.3"	40
	Correction of the numbering of the subtask "Funding decision of the first joint transnational call" from "ST3.2.4.1" to "ST3.2.4"	41
	Correction of the numbering of the task "Topic selection for the **second** joint transnational call" from "T3.1.2" to "T3.1_(2)"	41
	Correction of the numbering of the task "Joint Transnational call - **implementation** of the second call" from "T3.2.2" to "T3.2_(2)"	41
	Correction of the numbering of the subtask "Preparation of the **second** joint transnational call and establishment of the joint call secretariat" from "ST3.2.2.1" to "ST3.2.1_(2)"	41
	Removal of the following organisations from the Person-Month table of WP4 to comply with the budget distribution for Year 1: IT-MOH (76) , CSO-MOH (49)	42
	Precision of the contribution (in-kind) provided by the beneficiary "HRB (67)" the Person-Month table of WP4	42
	Harmonisation of Beneficiary acronym from UTartu to UTARTU	47, 111
	Harmonisation of Beneficiary acronym from GMS-Region Skane to GMS-RS	51
	Harmonisation of the precision of the affiliated entity in charge: from INSERM_CAD to CAD	51,94,95

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Harmonisation of Beneficiary acronym from Centogene to CENTOGENE	52
Removal of the following organisations from the Person-Month table of WP7 to comply with the budget distribution for Year 1: CIBER (125), UMCG (19), CUH (171), EURORDIS (26), INSERM _ Orphanet (1), CHU Dijon (46), UGENT (118), RS (65), GMS - RS (146), IBG (68), IMAGINE (70).	52
Correction of the number of the Associated partner "CUH*" to 171 in the Person-Month table of WP8	59
Removal of the following organisations from the Person-Month table of WP8 to comply with the budget distribution for Year 1: AMU (37), CNAG (10), IBG (68), OPBG (88), REGIONH (48)	59
Removal of the following organisations from the Person-Month table of WP9 to comply with the budget distribution for Year 1: INSERM (1), TUM (12)	64
Removal of the following organisations from the Person-Month table of WP10 to comply with the budget distribution for Year 1: MRT (79), CVBF (50), Sciensano (97), EURORDIS (26), QUB-UK* (173), RDI (34), UPPMD (120).	70
Harmonisation of Beneficiary acronym from ICS-VHIR to VHIR	71
Harmonisation of Beneficiary acronym from SCI to Sciensano	72
Addition of 105-FTELE in the efforts table Person-Months table) in the WP11 description.	73
Removal of the following organisations from the Person-Month table of WP11 to comply with the budget distribution for Year 1: UC (28), INSERM_ART-ARNm (1), INSERM_IT-GGB (1)	73
Addition of the beneficiary "FHG" that was missing in the contributing organisation list of task 11.3 "Design the proof-of-concept studies to evaluate the selected pipelines".	75
Removal of the following organisations from the Person-Month table of WP12 to comply with the budget distribution for Year 1: INSERM_U112 (UNISTRA) (1), UPPMD (120), SRUMC (11), FSJD-CERCA (60), UKLFR (115)	75
Harmonisation of Associated partner acronym from Roche/ Roche (Spartx) to ROCHE	79, 132
Removal of 128-UANTWERPEN in the efforts table (Person-Months table) in the WP13 and WP15 description.	80, 90
The duplication of the 'LUMC' organization in the listing of the contributors of task 13.1 "VP/Data Service Hub steering" has been removed.	84
Harmonisation of the precision of the Beneficiary unit acronym from INSERM-Orphanet to INSERM_Orphanet	84, 96
Correction of the acronym of the co-leading organization of task 13.2 "RD-VP evolution and scaling up" from UT to UTWENTE	85
Change of Beneficiary acronym from EMBL-EBI to CRG-CERCA	89
Harmonisation of Beneficiary acronym from C-Path to C-PATH	89
Removal of the following organisations from the Person-Month table of WP15 to comply with the budget distribution for Year 1: AIT (36)	90
Addition of 15-VHIR in the efforts table in the WP17 description.	101
Addition of VHIR as contributing beneficiary to tasks 17.1. "Execution of the Mentoring Program" (and its subtasks 17.1.1, 17.1.2 and 17.1.3) and 17.2 "Consultancy service".	103 - 104
Addition of Associated partner 159- Miltenyi in the contributors table	104
Removal of 105-TEDDY in the efforts table in the WP18 description.	104
Addition of Beneficiary 99- SFU in the contributors table	107

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Addition of the title of the subtask “ST23.2.1. NMG Responsibilities” (the subtask was described but it lacked the title)	107
Harmonisation of Beneficiary acronym from UHasselt to UHASSELT	110, 111
Harmonisation of Beneficiary acronym from UTwente to UTWENTE	111, 117
Removal of Beneficiary UCSC, named twice in T20.4	120
Update of person-months for 1-INSERM in the efforts table in the WP21 description.	122
Harmonisation of Associated partner acronym from Astra Zeneca to AZ	129
Correction of the acronym of the Associated Partner from “AstraZeneca” to “AZ” in subtask 21.2.6 and task 21.5	129, 133
Change of Associated partner acronym from FDB (Fujifilm) to FDB	130
Harmonisation of the precision of the Beneficiary unit acronym from Inserm_Target (Nantes) to INSERM_TARGET/NANTES	132
Harmonisation of the precision of the Beneficiary unit acronym: from Inserm-U974 to INSERM_U974	132, 14
Removal of the following organisation from the Person-Month table of WP23 to comply with the budget distribution for Year 1: UO (149)	137
Harmonisation of the precision of the Beneficiary unit acronym: from Inserm-IT-GGB to INSERM_IT-GGB	140
Harmonisation of Beneficiary acronym from the old acronym “GFGGRD” to GERAD the Person-Month table of WP24	146
Removal of the following organisations from the Person-Month table of WP25 to comply with the budget distribution for Year 1: TEAMIT (2), c4c-S (122), UKHD (13), UT (8), INSERM_IT-GGB (1)	149
Harmonisation of Beneficiary acronym from Sorbonne University to SU in the Person-Month table of WP25	149
Harmonisation of Associated partner acronym from Rare Care Centre to RCC in the Person-Month table of WP25	149
Update of the description of Beneficiary 24-APHP	167
Addition of the description of the new added beneficiary “150 – HSJD”	206
Update of the table listing the associated partners	215
Update of Table 2.3.d: Summary of staff effort for Year 1 (Leaders in bold) following EC request.	217-224
Update of Table 2.3.e: ‘Purchase costs’ items only with ‘Purchase costs’ items for Year 1 following EC request.	225-236

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	Harmonisation of Beneficiaries acronyms from ISCIII-IIER/ISCIII-SGIPRI to ISCIII; from CUH (NIHR-RDBR) to CUH; from UTartu to UTARTU; from ICS/ and ICS/VHIR to VHIR; from Astra Zeneca to AZ; from AMC or AUMC to AUMC; from Uhasselt to UHASSELT; from Centogene to CENTOGENE; from Copenhagen Economics to CE; from RS (GMS-GMCK) to RS; from MAPI Research Trust to MRT; from SCI to Sciensano; from GMS-Skane Region to GMS-RS; from Otago University to UO; from NIHDRJ to INSA; from Rare Care Centre to RCC; from Sorbonne University to SU; from Motol University to MUH; from GFGGRD to GERAD	NA
	Harmonisation of Beneficiary acronym from RS(GMS-GMCK) to RS	NA
	Removal of Table 2.3.d - Bis: Summary of staff effort for the three years (Leaders in bold) following EC request.	NA
	Update of the all the Associated Partners numbers following the addition of the beneficiary “155 – HSJD”. The associated Partners being after “155 – HSJD”, each of their number was thus increased by one (1).	NA
	Removal of the annex “Strategic Research and Innovation Agenda (SRIA)”	NA
30.05.2024	Harmonisation of Beneficiary acronym from UPPMD to WDO	17,22,24,28,34,36,38,41,42,43,44,46, 72,76,89,90,112,115,118,120,198
	Update of person-months for 2-TEAMIT in the efforts table in the WP2 and WP25 description.	29
	Update of person-months for 99-SFU in the efforts table in the WP20 description.	112
	Removal of UKA from WP20 tasks description and person-months	112-122
	Update of person-months for 86-RDG in the efforts table in the WP23 description.	138
	Update of Table 2.3.d: Summary of staff effort for Year 1	217
	Completion of the list of organisation mentioned as contributors next to the tasks 6.1, 6.2 and 6.3 to precisely indicate all the involved organisations.	50-52
	Update of the list of the organisations involved in tasks 9.1, 9.4 and 10.1 by adding the organisation “KUM” (the affiliated entity of the beneficiary “LMU”)	65, 67, 71
	Completion of the list of organisation mentioned as contributors next to the tasks 3.1 and 3.2 to precisely indicate all the involved organisations.	38-39
18.06.2024	Correction of the organisations list leading the task 21.1 by re-introducing 63-GNT as co-leader	127
	Correction of the organisations list leading the task 21.2 by re-introducing 55-FHG as co-leader	128
	Correction of the organisations list leading the task 21.3 by re-introducing 124-CNRS as co-leader	129
	Addition of 70-IMAGINE to the list of the organisations leading the task 21.4	131
	Update of the organisations list contributing to task 11.4	74

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18.06.2024	Transfert of budget (total cost: 31,475.00 € ; EC contribution: 163,327.50 €) from "1 INSERM _ Institut national de la santé et de la recherche médicale" to the Additional Beneficiary "59 IFD _ Innovation Fund Denmark". All management budget is taken from the WP3 CENTRAL BUDGET - Evaluation meetings JTCs2025/2026 (Other goods, work and services) and the funding budget is taken from the central enveloppe for JTCs at "1 INSERM". . Concerned work packages: WP1, WP3	NA
	Transfert of budget (total cost: 21,422.50 € ; EC contribution: 86,780.25 €) from "1 INSERM _ Institut national de la santé et de la recherche médicale" to the Additional Beneficiary "62 MZd/AZV _ Ministerstvo Zdravotnictvi Ceske Republiky" And Its Affiliated Entity "62.1 AZV _Czech Health Research Council". All management budget is taken from the WP3 CENTRAL BUDGET - Evaluation meetings JTCs2025/2026 (Other goods, work and services) and the funding budget is taken from the central enveloppe for JTCs at 1 INSERM. . Concerned work packages: WP1, WP3	NA
	Transfert of budget (total cost: 125,175.00 € ; EC contribution: 62,587.50 €) from "IBMT (Germany) that was Initially affiliated entity of 167- Fraunhofer UK" to "10 CNAG _ Consorcio Para La Explotacion Del Centro Nacional De Analisis Genómico". It is a budget for training and capacity building activity (WP20) managed by CNAG for further distribution (central budget). "IBMT" (the previous affiliated entity of Fraunhofer UK) was having this budget. IBMT withdrew and is not involved anymore in ERDERA. The task is transfered to WP Leaders until allocation of the task to another ERDERA Partner. Concerned work packages: WP20	NA
	Transfert of budget (total cost: 3,750.00 € ; EC contribution: 1,875.00 €) from "IBMT (Germany) that was Initially affiliated entity of 168- Fraunhofer UK" to "1 INSERM _ Institut national de la santé et de la recherche médicale". Initially located at IBMT (fraunhofer UK affiliated entity) for attenfing the ERDERA General Assembly meeting. This Budget is centralised at INSERM: budget for attending the ERDERA General Assembly meeting (central budget). All Organisations have the same budget for ERDERA General Assembly meeting participation. Concerned work packages: WP1	NA
	Transfert of budget (total cost: 268,667.50 € ; EC contribution: 134,333.75 €) from "170 UNEW_University Of Newcastle Upon Tyne" to "1 INSERM _ Institut national de la santé et de la recherche médicale". This Budget was initially centralised at UNEW to be allocated for Train the trainer model: personnel cost per National Training Provider to perform one training activity per country for the first three years of ERDERA. Transferred to INSERM (central budget). This budget is centralised at INSERM in WP23 because it was not directly allocated to University of Newcastle but to be reallocated later in the project to other ERDERA Partners. Concerned work packages: WP23	NA
	Transfert of budget (total cost: 77,850.00 € ; EC contribution: 38,925.00 €) from "1 INSERM _ Institut national de la santé et de la recherche médicale" to the Additional Beneficiary "90 JSI _ Institut Jozef Stefan". Budget transfer from central enveloppe located at Coordination "1 INSERM" for National Mirror Group Activities (WP23) and travel costs for the General Assembly meetings participation (WP1). Concerned work packages: WP1, WP23	NA
	Transfert of budget (total cost: 63,600.00 € ; EC contribution: 32,557.50 €) from "1 INSERM _ Institut national de la santé et de la recherche médicale" to the Additional Beneficiary "149 UO _ University of Otago". Budget transfer from central enveloppe located at Coordination "1 INSERM" for National Mirror Group Activities (WP23), the Clinical Research Network Diagnostic Reseach Stream (WP6) and travel costs for the General Assembly meetings participation (WP1). Concerned work packages: WP1, WP6, WP23	NA
	Transfert of budget (total cost: 52,500.00 € ; EC contribution: 26,250.00 €) from "1 INSERM _ Institut national de la santé et de la recherche médicale" to the Additional Beneficiary "148 IPG _ Institut de Pathologie et de Génétique" in Belgium (Wallonian Part added to address request from Member State representative). Budget transfer from central enveloppe located at Coordination "1 INSERM" for Clinical Research Network Diagnostic Reseach Stream (WP6) and travel costs for the General Assembly meetings participation (WP1). Concerned work packages: WP1, WP6	NA

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	Transfert of budget (total cost: 51,250.00 € ; EC contribution: 25,625.00 €) from "147 VIB _ Vlaams Instituut Biotechnologie Flanders Institute For Biotechnology" to the Additional Beneficiary "128 UANTWERPEN _ Universiteit Antwerpen". Part of the Budget from "VIB" transferred to "UANTWERPEN" (as per their request). VIB is a Belgian partner (Flammish part). Concerned work packages: WP1, WP6	NA
	Transfert of budget (total cost: 124,312.50 € ; EC contribution: 62,156.25 €) from the removed organisation "PMU _ PARACELSUS MEDIZINISCHE PRIVATUNIVERSITAT SALZBURG - PRIVATSTIFTUNG _ Austria" to "141 PLUS _ PARIS-LONDON-UNIVERSITAT SALZBURG". The Principal Investgator initially at "PMU", and the only one performing the tasks described (WP19: Methodological Support), moved to "PLUS". The budget related to this task is transferred to "PLUS". "PMU" is terminated as no task left for this partner to be performed in ERDERA. Concerned work packages: WP19	NA
	Transfert of budget (total cost: 3,750.00 € ; EC contribution: 1,875.00 €) from the removed organisation "PMU _ PARACELSUS MEDIZINISCHE PRIVATUNIVERSITAT SALZBURG - PRIVATSTIFTUNG _ Austria" to "1 INSERM _ Institut national de la santé et de la recherche médicale". Following the termination of "PMU", the travel budget for attending the ERDERA General Assembly meetings is transferred to Coordination "1 INSERM" (central budget). Concerned work packages: WP1	NA
	Transfert of budget (total cost: 112,350.00 € ; EC contribution: 56,175.00 €) from "1 INSERM _ Institut national de la santé et de la recherche médicale" to the Additional Beneficiary "85 MoH SR _ Slovakian Ministry of Health". Budget transfer from central enveloppe located at Coordination "1 INSERM" for National Mirror Group Activities (WP23) and travel costs for the General Assembly meetings participation (WP1). Concerned work packages: WP1, WP23	NA
	Transfert of budget (total cost: 79,850.00 € ; EC contribution: 39,925.00 €) from "1 INSERM _ Institut national de la santé et de la recherche médicale" to the Additional Beneficiary "86 RDG _ Rare Diseases Greece". Budget transfer from central enveloppe located at Coordination "1 INSERM" for National Mirror Group Activities (WP23) and travel costs for the General Assembly meetings participation (WP1). Concerned work packages: WP1, WP23	NA
	Transfert of budget (total cost: 135,000.00 € ; EC contribution: 67,500.00 €) from "22 EATRIS _ European Infrastructure for Translational Medicine _ Europe" to "15 VHIR _ Vall d'Hebron Research Institute_Spain". "EATRIS" would transferred the equivalent of 6PM/Y (18PM) to "VHIR" for implementing activities under WP17 - Initiation of Mentoring process and feasibility study for consultancy services. "VHIR" was already an affiliated partner of EATRIS under "EJP RD WP19" and has provided key capacities in the setting-up, piloting and deployment of mentoring support. Under ERDERA, it is key to build on the experience draw from the first partnership for an efficient execution of the mentoring programme in place under WP17. Key to the WP the Innovation Management ToolBox. Initially developed under EJP RD with "VHIR" as lead manager for that effort, "VHIR" will allow to retain knowledge and perform maintenance activities foreseen. Concerned work packages: WP17	NA
	Transfert of budget (total cost: 108,558.125 € ; EC contribution: 54,279.0625 €) from "140 PEI _ Bundesinstitut Fur Impfstoffe Und Biomedizinische Arzneimittel (Paul-Ehrlich-Institut) _ Germany" to "55 FHG _ Fraunhofer Gesellschaft Zur Forderung Der Angewandten Forschung EV". One of the researchers involved at PEI is joining FHG and will perform his tasks at his new institution. Concerned work packages: WP21	NA
	Transfert of budget (total cost: 73,125.00 € ; EC contribution: 36,562.50 €) from the removed organisation "Vejle Hospital_Vejle Hospital, Sygehus Lillebælt" to "87 REGIONSYD_Region Syddanmark". Following "Vejle Hospital" internal decision "Vejle Hospital" is terminated. Activity and budget in WP6 is transferred to "87 REGIONSYD". Concerned work packages: WP6	NA
	Transfert of budget (total cost: 3,750.00 € ; EC contribution: 1,875.00 €) from the removed organisation "Vejle Hospital_Vejle Hospital, Sygehus Lillebælt" to "1 INSERM _ Institut national de la santé et de la recherche médicale". Following "Vejle Hospital" internal decision "Vejle Hospital" is terminated. Travel budget to ERDERA General assembly meetings participation is centralised at Coordination "1 INSERM" (central budget). Concerned work packages: WP1	NA

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	Transfert of budget (total cost: 65,000.00 € ; EC contribution: 32,500.00 €) from "60 FSJD-CERCA_Fundacio Privada Per A La Recerca I La Docencia Sant Joan De Deu" to the Additional Beneficiary "150 HSJD_Hospital Sant Joan De Deu". Upon request of these two organisations, "HSJD" is added as beneficiary and not as affiliated entity of "FSJD-CERCA". The budget was initially planned under beneficiary "60 FSJD-CERCA" to "HSJD". Concerned work packages: WP1, WP25	NA
	The budget for the first two JTCs from "7 ZonMw _ Zorgonderzoek Nederland Zon" will be 1.8 million € per Call, thus 3.6 million € in total for the first 3 years of ERDERA. Previously it was 2 million € per call. Consequently, there is a reduction of 400 000 € in WP3 for "7 ZonMw".	NA
	Transfert of budget (total cost: 3,750.00 € ; EC contribution: 1,875.00 €) from the removed organisation "Luni_UNIVERSITE DE LILLE" to "1 INSERM _ Institut national de la santé et de la recherche médicale". Following "Luni" internal decision, this initial beneficiary decided to withdraw from ERDERA. The initial budget planned to attend the ERDERA General Assembly meetings is transfered back to "1 INSERM" Coordination. Concerned work packages: WP1	NA
	Transfert of budget (total cost: 12,187.50 € ; EC contribution: 6,093.75 €) from the removed organisation "Luni_UNIVERSITE DE LILLE" to "10 CNAG _ Consorcio Para La Explotacion Del Centro Nacional De Analisis Genómico". Following "Luni" internal decision, this initial beneficiary decided to withdraw from ERDERA. The initial budget planned in task 20.4 is transfered back to the task Leader "CNAG" to be reallocated (central budget). Concerned work packages: WP20	NA
	Transfert of budget (total cost: 716,000.00 € ; EC contribution: 358,000.00 €) from "1 INSERM _ Institut national de la santé et de la recherche médicale" to its Affiliated Entity "1.1 CAD_Collecteur Analyseur de Données". Following the creation of legal entity Collecteur Analyseur de Données, "CAD" is added as affiliated entity of "INSERM". All budget (personnel costs) initially planned at "INSERM (CAD)" is transferred to the now Affiliated Entity "1.1 CAD". Concerned work packages: WP6, WP7, WP15	NA
	Transfert of budget (total cost: 113,296.40 € ; EC contribution: 56,648.20 €) from "114 UKA_ Universitaetsklinikum Aachen (Germany)" to "99 SFU_ Sigmund Freud Privatuniversitat Wien GMBH". Upon request of these two beneficiaries, the responsibilities for the subtasks relating to the budget transfer, i.e., 20.3.4 and 20.4.1 are transferred from "UKA" to "SFU" which has the capacity to take over. Concerned work packages: WP20	NA
	Transfert of budget (total cost: 5,000.00 € ; EC contribution: 2,500.00 €) from "54 F.R.S.-FNRS_FONDS DE LA RECHERCHE SCIENTIFIQUE- FNRS" to "1 INSERM _ Institut national de la santé et de la recherche médicale". Following the European Commission comments provided during the Grant Agreement Preparation, the budget related to the preparation and production of Certificate of Financial Statement (CFS) are transfered to coordinator for operations budget (e.g., Future unforeseen partners costs like CFS, etc.). Concerned work packages: WP1	NA
	Transfert of budget (total cost: 5,000.00 € ; EC contribution: 2,500.00 €) from "61 FCT _FUNDACAO PARA A CIENCIA E A TECNOLOGIA" to "1 INSERM _ Institut national de la santé et de la recherche médicale". Following the European Commission comments provided during the Grant Agreement Preparation, the budget related to the preparation and production of Certificate of Financial Statement (CFS) are transfered to coordinator for operations budget (e.g., Future unforeseen partners costs like CFS, etc.). Concerned work packages: WP1	NA
	Transfert of budget (total cost: 5,000.00 € ; EC contribution: 2,500.00 €) from "62.1 AZV_Czech Health Research Council" to "62 MZd _ MINISTERSTVO ZDRAVOTNICTVI CESKE REPUBLIKY". Following the European Commission comments provided during the Grant Agreement Preparation, the budget related to the preparation and production of Certificate of Financial Statement (CFS) is transferred to the main beneficiary "MZd" that is requesting more than 430,000.00€ EC Contribution. Concerned work packages: WP1	NA
	Transfert of budget (total cost: 5,000.00 € ; EC contribution: 2,500.00 €) from "109 RT (TuscReg)_REGIONE TOSCANA" to "1 INSERM _ Institut national de la santé et de la recherche médicale". Following the European Commission comments provided during the Grant Agreement Preparation, the budget related to the preparation and production of Certificate of Financial Statement (CFS) are transfered to coordinator for operations budget (e.g., Future unforeseen partners costs like CFS, etc.). Concerned work packages: WP1	NA

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	Transfert of budget (total cost: 5,000.00 € ; EC contribution: 2,500.00 €) from "138 FNR_FONDS NATIONAL DE LA RECHERCHE" to "1 INSERM _ Institut national de la santé et de la recherche médicale". Following the European Commission comments provided during the Grant Agreement Preparation, the budget related to the preparation and production of Certificate of Financial Statement (CFS) are transfered to coordinator for operations budget (e.g., Future unforeseen partners costs like CFS, etc.). Concerned work packages: WP1	NA
	Transfert of budget (total cost: 5,000.00 € ; EC contribution: 2,500.00 €) from "139 NKFIH_NEMZETI KUTATASI FEJLESZTESI ES INNOVACIOS HIVATAL" to "1 INSERM _ Institut national de la santé et de la recherche médicale". Following the European Commission comments provided during the Grant Agreement Preparation, the budget related to the preparation and production of Certificate of Financial Statement (CFS) are transfered to coordinator for operations budget (e.g., Future unforeseen partners costs like CFS, etc.). Concerned work packages: WP1	NA
	Transfert of budget (total cost: 5,000.00 € ; EC contribution: 2,500.00 €) from "144 Vinnova_VERKET FOR INNOVATIONSSYSTEM" to "1 INSERM _ Institut national de la santé et de la recherche médicale". Following the European Commission comments provided during the Grant Agreement Preparation, the budget related to the preparation and production of Certificate of Financial Statement (CFS) are transfered to coordinator for operations budget (e.g., Future unforeseen partners costs like CFS, etc.). Concerned work packages: WP1	NA

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List of Abbreviations

Acronym	Full name
1+MG	1+ Million Genome initiative
1M1M	1 mutation 1 medicine (initiative)
AAV	Adeno-Associated Virus
ACT EU	Accelerating Clinical Trials in the European Union
ADPKD	Autosomal Dominant Polycystic Kidney Disease
AI	Artificial Intelligence
AIM-IMA	Agence InterMutualiste
API	Application Programming Interface
ARCA	Autosomal Recessive Cerebellar Ataxia
ASO	Antisense Oligonucleotides
ASTERIX	Advances in Small Trials dEsign for Regulatory Innovation and eXcellence
ATMP	Advanced Therapy Medicinal Product
AWP	Annual Work Programme
AWP1	Annual Work Plan Year 1
AWP2	Annual Work Plan Year 2
AXD	Alexander Disease
B1MG	Beyond 1 Million Genomes
BGTC	Bespoke Gene Therapy Consortium
BM	Business Model
BMC	Business Model Canvas
BNDMR	French National Rare Disease Registry
BoD	Burden Of Diseases
BoF	Board of Funders
BSEP	Bile Salt Export Pump
BYOD	Bring Your Own Data
C&D	Communication and Dissemination
CA	Consortium Agreement
CDA	Confidential Disclosure Agreement
CDISC	Clinical Data Interchange Standards Consortium
CDM	Common Data Model
cDNA	complementary DNA
CHMP	Committee for Medicinal Products for Human Use
CITEseq	Cellular Indexing of Transcriptomes and Epitopes by Sequencing
ClinRO	Clinician-Reported Outcome
CNV	Copy Number Variation
COA	Clinical Outcome Assessment
COI	Cost of Illness
Coo	(ERDERA) Coordination (team)
COST	European Cooperation in Science and Technology
CRN	Clinical Research Network

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Acronym	Full name
CS	Clinical Studies
CSC	Call Steering Committee
CT	Clinical Trial
CTEB	Clinical Trial Evaluation Board
CTO	Chief Technology Officer
CTSC	Clinical Trial Scientific Committee
CWL	Common Workflow Language
D	Deliverable
DALY	Disability-Adjusted Life Years
DARWIN	Data Analysis and Real World Interrogation Network
DATF	Data Analysis Task Force
DDD	Dense Deposit Disease
DDT	Drug Development Tools
DG CONNECT	Directorate-General for Communications Networks, Content and Technology
DG JRC	Directorate-General Joint Research Center
DG RTD	Directorate-General for Research and Innovation
DG SANTE	Directorate-General for Health and Food Safety
DH	Data Hub
DITF	Data Interpretation Task Force
DMD	Duchenne Muscular Dystrophy
DMP	Data Management Plan
DNA	Deoxyribonucleic Acid
DSB	DNA Double-Strand Break
DSH	Data Services Hub
DSW	Data Stewardship Wizard
EAG	Ethics Advisory Group
EATRIS	European infrastructure for translational medicine
EBI	European Bioinformatics Institute
EC	European Commission
ECRIN	European Clinical Research Infrastructure Network
ECTS	European Credit Transfer and Accumulation System
EFPIA	European Federation of Pharmaceutical Industries Associations
EGA	European Genome-Phenome Archive
EHDS	European Health Data Space
EHR	Electronic Health Record
EHR4CR	Electronic Health Records for Clinical Research
EJP RD	European Joint Programme on Rare Diseases
ELISA	enzyme-linked immunosorbent assay
ELSA	Ethical, Legal and Social Aspects
ELSI	Ethical, Legal, and Social Issues
EMA	European Medicines Agency
EO	Expected Outcome

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Acronym	Full name
EOSC	European Open Science Cloud
ePAGs	European Patient Advocacy Groups
EPAs	Entrustable Professional Activities
ERA4Health	Fostering a European Research Area for Health Research
ERC	European Research Council
ERDERA	European Rare DisEases Research Alliance
ERICA	The European Rare Disease Research Coordination and Support Action consortium
ERKNet	European Reference Network on kidney diseases
ERKReg	The European Rare Kidney Disease Registry
ERN	European Reference Network
ERN CRANIO	ERN on craniofacial anomalies and ear, nose and throat (ENT) disorders
ERN GENTURIS	ERN on genetic tumour risk syndromes
ERN-EpiCARE	ERN on epilepsies
ERN-ERNICA	ERN for rare Inherited and Congenital Anomalies
ERN-EuroBloodNet	ERN on haematological diseases
ERN-ITHACA	European Reference Network on congenital malformations and rare intellectual disability
ERN-RDN	ERN on neurological diseases
ERN-RITA	ERN on immunodeficiency, autoinflammatory and autoimmune diseases
ESFRI	European Strategy Forum on Research Infrastructures
ESHG	European Society of Human Genetics
EU	European Union
EUCOPE	European Confederation of Pharmaceutical Entrepreneurs
EUHA	European University Hospital Alliance
EuReCA	EU Resource Efficiency Coordination Action
EURO-NMD	European Reference Network for Rare Neuromuscular Diseases
EVs	Extracellular Vesicles
ExCom	Executive Committee
F2F	Face-to-Face
FAIR	Findable, Accessible, Interoperable, Reusable
FDA	U.S. Food and Drug Administration
FHIR	Fast Healthcare Interoperability Resource
FP	Framework Programme
GA4GH	Global Alliance for Genomic Health
GB	Governing Board
GCLP	Good clinical laboratory practice
GCP	Good Clinical Practice
GDI	Genomic Data Infrastructure
GDPR	General Data Protection Regulation
GenoMed4All	Genomics and Personalized Medicine for all
GMP	Good Manufacturing Practice
GMS	Genomic Medicine Sweden

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Acronym	Full name
GO	General Objective
GoF	Gain of Function
GPAP	Genome Phenome Analysis Platform
HCP	Health Care Practitioner
HDR	Homology Directed Repair
hE	human Embryos
HER	Health Electronic Record
hESC	human embryonic stem cells
HGVS	Human Genome Variation Society
HITI	Homology-Independent Targeted Integration
HOOM	HPO-ORDO Ontological Module
HPO	Human Phenotype Ontology
HSPC	Hematopoietic Stem and Progenitor Cells
HTA	Health Technology Assessment
i.p.	Intraperitoneal injection
ICF	International Classification of Functioning, Disability and Health
ICT	Innovative Cellular Therapeutics
IDEAL	Integrated DEsign and AnaLysis of clinical trials in small population group
IEA	Independent Ethics Advisor
IHI	Innovative Health Initiative
IMT	Innovation Management Toolbox
InSPiRe	Innovative methodology for small populations research
IP	Intellectual Property
IPR	Intellectual Property Rights
iPSC	induced Pluripotent Stem Cells
IRDiRC	International Rare Diseases Research Consortium
ISA	Investigation, Study and Assay
IT	Information Technology
ITR	Inverted Terminal Repeat sequences
IV	Intravenous
JARDIN	Joint Action for Integration of ERNs
JCS	Joint Call Secretariat
JRC	Joint Research Centre
JTC	Joint Transnational Call
KPI	Key Performance Indicator
LNP	Lipid Nanoparticles
LOINC	The international standard for identifying health measurements, observations, and documents
LRS	Long-Read Sequencing
LS AAI	Life Science Authentication and Authorization Infrastructure
M	Month
MAB	Multistakeholder Advisory Board

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Acronym	Full name
MAxO	Medical Action Ontology
MEI	Mobile Element Insertions
metabERN	European Reference Network on hereditary metabolic disorders
mHEALTH	Mobile health solutions
MHLW	Japanese Ministry of Health, Labour and Welfare
ML	Machine Learning
MoU	Memoranda of Understanding
MRI	Magnetic Resonance Imaging
mRNA	Messenger Ribonucleic Acid
MS	Member States
mtDNA	Mitochondrial Deoxyribonucleic Acid
NAB	National Alignment Board
NBS	Newborn Screening
NGO	Non-Governmental Organization
NGS	Next Generation Sequencing
NHEJ	Non-Homologous End Joined
NIH	National Institutes of Health
NLP	Natural Language Processing
NMG	National Mirror Group
NP	National Plan
NSHS	National System of Health Data
NSS	Networking Support Scheme
NTP	National Training Provider
OA	EURORDIS Open Academy
ObsRO	Observer Reported Outcome
ODD	Orphan Drug Designation
OFCO	Orphanet Functional Consequences Ontology
OG	Operating Group
OGM	Optical Genome Mapping
OMIM	Online Mendelian Inheritance in Man
OMOP	Observational medical outcomes partnership
OMP	Orhan Medicinal Product
OO	Operational Objective
ORDO	Orphanet Rare Disease Ontology
p-medicine	Personalised Patient Information for Clinical Decision Support
PAES	Post-Authorization Efficacy Studies
PAO	Patient Advocacy Organization
PASS	Post-Authorization Safety Surveillance
PBMC	Peripheral Blood Mononuclear Cells
PCR	Polymerase Chain Reaction
PerfO	Performance Outcomes
PLWRD	People Living With a Rare Disease

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Acronym	Full name
PMDA	Japanese Pharmaceuticals and Medical Devices Agency
PPIE	Patient and Public Involvement and Engagement
PREMs	Patient-Reported Experience Measures
PRO	Patient Reported Outcome
PROMs	Patient Reported Outcome Measures
QC	Quality Control
QoL	Quality of Life
QSAR	Quality Structure Activity Relationship
R&I	Research and Innovation
rAAV	recombinant Adeno-Associated Virus
RADeep	Rare Anaemia Disorders European Epidemiological platform
RD	Rare Disease(s)
RDCA-DAP	The C-Path Rare Disease Cures Accelerator-Data and Analytics Platform
REAL	Re-Analysis Logistics
RESTORE	Large Scale Research Initiative in Europe
RNA	Ribonucleic Acid
RNA-seq	RNA sequencing
RRI	Responsible Research and Innovation
RSG	Regulatory Support Group
RWD	Real World Data
RWE	Real World Evidence
SAWP	Scientific Advice Working Party
SB	Sleeping Beauty
SC	Steering Committee
sc-RNA	Single Cell RNA
SCD	Sickle Cell Disease
SciSec	IRDiRC Scientific Secretariat
scRNA-seq	Single Cell RNA sequencing
SEC	Scientific Evaluation Committee
SMA	Spinal Muscular Atrophy
SME	Small and Medium Enterprise
SNP	Single-Nucleotide Polymorphism
SO	Specific Objective
SOA	Service-Oriented Architecture
Solve-RD	Solving the Unsolved Rare Diseases
SOP	Standard Operating Procedure
SPAX	Spastic Ataxia Diseases
SPE	Secure Processing Environment
SRIA	Strategic Research and Innovation Agenda
SSSOM	Simple Standard for Sharing Ontological Mappings
ST	Sub-Task
STL	Sub-Task Leader

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Acronym	Full name
STR	Short Tandem Repeat
SV	Structural Variant
SWOT	strengths, weaknesses, opportunities, threats
T	Task
T2T	Telomer-to-Telomer
TCRseq	T Cell Receptor Sequencing
TF	Task Force
TL	Task Leader
TRANSFoRm	Translational Research and Patient Safety in Europe
TRE	Trusted Research Environments
UC	Underrepresented Countries
UDN	Undiagnosed Disease Networks
UDP	Undiagnosed Rare Disease Programs
UI	User Interface
USA	United States of America
UX	User Experience
VLPs	Virus-Like Particles
VP	Virtual Platform
VUS	Variant of Unknown Significance
WG	Working Group
WHO	World Health Organization
WP	Work Package
WS	Work Stream
YPAG	Young Persons Advisory Group

1. Excellence #@REL-EVA-RE@#

1.1. Objectives and ambition of the Partnership #@PRJ-OBJ-PO@#

1.1.1 Europe's journey and commitment to Rare Diseases

Today, there are about **7000 rare diseases (RDs) affecting more than 300 million people worldwide** including 30 million in Europe[1]. In the European Union, a disease is considered as rare when it affects not more than 1 person in 2,000[2]. Many RDs manifest in childhood, affecting a patient's entire life and are not treatable with current interventions or medications. Indeed, 95% of RDs are without any therapeutic option[3]. Furthermore, RDs have low, or extremely low prevalence, lack natural history studies, and even where the genetic origin may be known, there is often a severe lack of knowledge of the downstream pathophysiological mechanisms for conventional drug intervention and heterogeneity of the affected populations. About 50% of rare disease patient do not have a confirmed molecular diagnosis[4,5] and the average time for diagnosing a known rare disease is still more than 4 years. Furthermore, 52% of patients and carers confirm that their disease has a severe or highly severe impact on daily life[6]. For these reasons, RDs, resulting in high medical need and significant costs, remain challenging for both health care systems and for potential investors, as witnessed by the lack of available therapies and delayed diagnosis. For the same reasons, rare diseases are recognised as an unparalleled field where European and international collaboration is indispensable.

Rare diseases were nearly invisible in our health and social care systems in previous decades. Today, they are recognised as a public health and human rights priority in large part due to a policy framework in Europe[7]. For years, many stakeholders in Europe, with the support of the European Union, have contributed to building a cohesive RD ecosystem. New avenues for the RD community are now open since the launch in the last 2 decades of important RD initiatives: the resource platform Orphanet, and of the patients' organisation EURORDIS ('97), the adoption of a European legislation on medicines for rare diseases ('99-2000) and children[8] (2006-2007), the adoption of the Council Recommendation on European Action in the field of Rare Diseases[9] (2009), the establishment of the International Rare Diseases Research Consortium (IRDiRC) (2011), the recent implementation of the European Reference Networks (ERNs) (2017) set up thanks to the Directive on patients' rights in cross-border healthcare (2011), the launch of the European Platform for Rare Disease Registration (2018), the creation of the European Joint Programme on Rare Diseases (EJP RD) (2019), the evaluation on the legislation for medicines for rare diseases and for children (2020) and initiatives to evaluate and improve the European Orphan Medicinal Product landscape (2021), and, last but not least, launch of the RD Moonshot (2022) first public-private coalition fostering the acceleration of drug development pathway. At national level many European countries adopted national plans (NP) and/or national strategies (NS) to tackle rare diseases[10], including some policies for research. At EU level, these endeavours were supported by EU funding such as the EU Health Programmes and the Research FPs, as the so-called ERA-Net scheme (networking of national research funding agencies): E-Rare-1, E-Rare-2 and E-Rare-3, predecessors of EJP RD.

From the scientific standpoint, the recent acceleration of new technologies and development of advanced therapeutic medicinal products (ATMPs) has opened new opportunities for many genetic diseases offering first-time treatments tackling the root causes of the disease and potentially even a cure[11] as opposed to traditional treatments which are focused largely on treating symptoms only. Recently, platform approaches and strategies have become a more efficient and common to address new treatment or diagnostics development including clinical trials. To that end, in 2021, the National Institute of Health (NIH) in the US, together with the U.S. Food and Drug Administration (FDA), as well as multiple pharmaceutical companies and non-profit organizations, launched the Bespoke Gene Therapy Consortium (BGTC) aiming at establishment of platforms and standards to speed up the development and delivery of customized or "bespoke" gene therapies that could treat millions of people affected by rare diseases, including diseases too rare to be commercially viable. At the same time in Europe, initiatives like RESTORE[12] or RARE-IMPACT[13] contributed to gaining a better understanding of the European setting for ATMP development and delivery. Furthermore, the use of big data, implementation of FAIR principles, innovation beyond omics and artificial

[1] Nguengang Wakap et al., «Estimating Cumulative Point Prevalence of Rare Diseases».
[2] Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products; https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32000R0141&from=EN
[3] Kaufmann, Pariser, y Austin, «From scientific discovery to treatments for rare diseases – the view from the National Center for Advancing Translational Sciences – Office of Rare Diseases Research».
[4] Wise AL, Manolio TA, Mensah GA, et al. Genomic medicine for undiagnosed diseases. Lancet. 2019;394(10197):533-540. doi:10.1016/S0140-6736(19)31274-7
[5] Smith HS, Swint JM, Lalani SR, et al. Clinical Application of Genome and Exome Sequencing as a Diagnostic Tool for Pediatric Patients: a Scoping Review of the Literature. Genet Med. 2019 Jan; 21(1):3-16.
[6] Rare Barometer survey (May 2017): http://download2.eurordis.org.s3.amazonaws.com/rbv/2017_05_09_Social%20survey%20leaflet%20final.pdf
[7] Quote from Executive summary of Rare2030 Foresight in Rare Disease policy- Recommendations (Feb 2021)
[8] Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use; https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32006R1901
[9] https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF
[10] http://www.europlanproject.eu/NationalPlans?idMap=1
[11] «Realizing the promise of gene therapy through collaboration and partnering: Pfizer's view».(https://www.nature.com/articles/d42473-018-00307-6)
[12] «RESTORE - Large Scale Research Initiative in Europe». (https://www.restore-horizon.eu/)
[13] Rare Impact, «Rare Impact». (https://rareimpact.eu/)

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intelligence (AI), introduce additional opportunities[14]. Out of necessity rare diseases have become pioneers in tomorrow's transformations and creative solutions for research and healthcare. For example, the specificity of RDs (limited number of patients, their willingness to share their data [95%][15] and the scarcity of knowledge and expertise) as well as the structuration of RD ecosystem are the best rationale for data-driven solutions (e.g. EU Health Data Space and European Open Science Cloud) that will improve life of all EU citizens. Moreover, the rare diseases community continuously monitor progress towards the vision and mission of its programmes and instruments, and update them through a range of strategic studies including, but not limited to, the Rare 2030 Foresight in Rare Disease Policy (2021)[16], the IRDiRC State of play report (2019-2021)[15], and the scoping papers and state of play analyses that maps the research and innovation needs[17], analyse the alignment of the national plans and strategies for rare diseases[18] with EJP RD.

1.1.2 Ambition and Mission

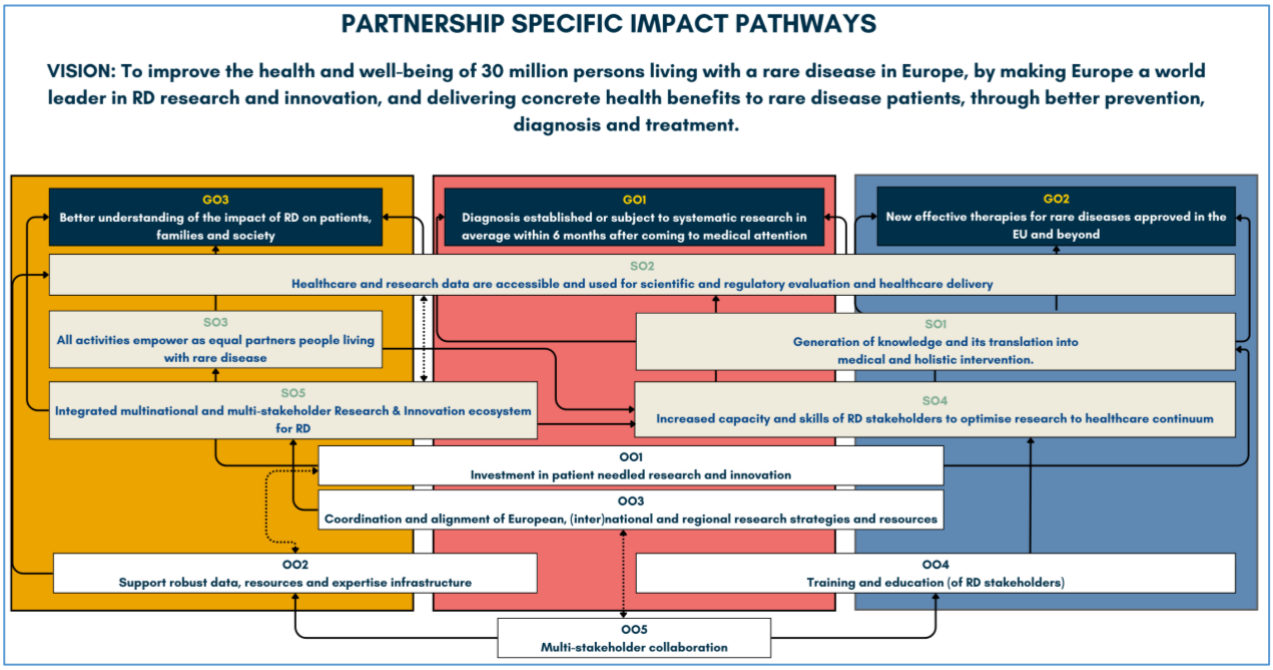
The **AMBITION** of ERDERA is to **improve the health and well-being of the 30 million people living with a rare disease in Europe, by making Europe a world leader in RD research and innovation, to support concrete health benefits to rare disease patients, through better prevention, diagnosis and treatment**. The Partnership will **deliver a RD ecosystem** that builds on the successes of previous programmes by supporting robust patient need-led research, developing new diagnostic methods and pathways, spearheading the digital transformational change connecting the dots between care, patient data and research, while ensuring strong alignment of strategies in RD research across countries and regions. Structuring goal-oriented public-private collaborations targeted at interventions all along the R&D value chain will ensure that the journey from knowledge to patient impact is expedited, thereby optimising EU innovation potential in RD. This will be enabled by a **tripartite MISSION** to be accomplished by 2034: (1) Bring to bear the high value, sustainable, supporting services from across Europe under one roof so that every high-quality RD research project will benefit from cross-disciplinary expertise, goal-oriented study planning and efficient execution; (2) Boost clinical study readiness of RDs by enabling every consenting patient living with a rare disease to be findable and enrolled in a suitable clinical study that is necessary for having regulatory and FAIR-principles compliant data sets, generating advances in diagnosis, understanding of diseases and developing treatments, (3) Make Europe a global leader in rare disease research through a significant increase in investment to spur innovation, by aligning the regional, national and European research and innovation priorities, leading to job creation and improving EU competitiveness in R&I.

1.1.3 Partnership's Objectives

[14] IRDiRC State of play report (2019-2021) (https://www.calameo.com/belevottomuus/read/0070392840140e96259d3)
[15] Rare Barometer survey (Jan 2020): http://download2.eurordis.org.s3.amazonaws.com/rbv/20-01-24%20RB%20Data%20Survey%20Fact%20Sheet_Final.pdf
[16] Rare 2030 Foresight in Rare Disease Policy (https://www.rare2030.eu/)
[17] D2.08 (link), D2.09 (link), D2.10 (link), D2.11 (link): First to Fourth EJP RD Scoping Paper
[18] D2.21 (link), D2.22 (link), D2.23 (link) and D2.24 (link): First to Fourth EJP RD Analysis of national state of play and alignment process with EJP RD

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The objectives of ERDERA are represented at three levels and organized according to the Partnership Specific Impact Pathways (PSIPs) (fig. 1). The **General Objectives (GOs) correspond to the long-term impacts** to which ERDERA aims to contribute. The **Specific Objectives (SOs)** reflect medium-term timescale and **correspond directly to the expected outcomes** that the Partnership should achieve or contribute to, in line with its mission, and within its lifetime or, at the latest, at 2034 horizon. Finally, the **Operational Objectives (OOs) are considered as means and resources** and are translated through the activities that will be implemented by the Partnership to accomplish the overarching SO and GO levels.



The General Objectives (GOs) are defined in line with the Partnership's vision and mission. It was agreed that they should be inspired by and fully aligned with the goals of IRDiRC.

Figure 1. Partnership Specific Pathways of ERDERA. The interlinks at each level exist: one SO may respond to more than one expected GO. The PSIP represents the most important (strongest) pathways that were agreed during the ERDERA SRIA development after the consultation of SRIA Task Force (more than 80 independent experts) and aggregating more than 500 pathways designed by its individual members.

GO1: Diagnosis established or enrolment in systematic research in average within 6 months after coming to medical attention (in EU and Associated countries)

Patients with undiagnosed diseases and their families often face an uncertain and unpredictable journey, called a diagnostic odyssey. ERDERA will contribute to shortening the diagnostic pathway for patients with rare diseases by decreasing time to diagnosis after the first medical appointment with a specialist for those disorders already identified in the literature. For the undiagnosed disorders efforts will be made to build and/or strengthen the bridge between research and healthcare to provide to every undiagnosed patient the possibility to be included in a globally coordinated diagnostic and research pipeline.

GO2: New effective therapies for rare diseases approved in the EU and beyond:

95% of RDs are still underserved in terms of research and patients with rare diseases, although diagnosed, face a lack of viable long-term treatment options. To contribute to IRDiRC Goal 2 – "1000 new therapies for rare diseases will be approved", ERDERA will accelerate the development of new therapies (especially for diseases without approved options) by providing the necessary expertise and technological support to research projects aimed at developing new effective treatments (encompassing drugs and innovative devices) and by expediting clinical trial readiness of rare diseases, including contribution to regulatory fitness to enable regulatory approval.

GO3: Better understanding of the impact of RDs on patients, families and society

Understanding of the impact of RDs on people lives means also better evaluation of the societal and healthcare costs and capacity to implement more inclusive, holistic healthcare approaches. Through required means (funding, data collection, education, awareness raising) and processes (involvement of PLWRD, public engagement) the Partnership will contribute to capturing of RD impact and comprehensive understanding of patients and carers needs leading to more impactful research and, in the

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long term, improved and/or new processes that will facilitate the diagnosis and care pathways and translate into meaningful societal support.

SO1: Generation of knowledge and its translation into medical intervention

The Partnership will enable patient-need led relevant science by providing a RD research support pipeline from basic research to clinical trial readiness. Attention will be paid to Social Sciences and Humanities research to better understand the impact of rare diseases and the potential benefit of new interventions. The integration across value chain will be addressed by combining research financed and performed by both public and private stakeholders and involving patients.

SO2: Healthcare and research data are accessible and used for scientific and regulatory evaluation & healthcare delivery

ERDERA will support the generation, pooling, integration and sharing of high-quality and interoperable RD data in an expanding ecosystem of distributed FAIR data sources, building on existing infrastructures encompassing ERDRI, the EJP RD Virtual Platform, RD-Connect, and services not specific for RD (e.g., BBMRI-ERIC). It will promote advanced data analysis and data interpretation methods and approaches (both federated and centralised) that exploit this ecosystem. It will support the development of data-driven computational tools, statistical and AI methods, as well as digital solutions to understand the diseases progression, to solve undiagnosed RD cases and implement new clinical studies/trials designs for small populations.

SO3: All activities empower, as equal partners, people living with rare diseases

The Partnership will provide an inclusive pathway and adequate resources to empower PLWRD and/or representatives as equal partners. PLWRD will be involved at all levels of governance and execution of ERDERA, with training or induction as necessary. A structured and flexible framework for patient engagement in research (including funding) will be developed and will promote best practices, re-using and extending existing resources. To reduce inequities between different types of RD, underserved RDs will be targeted through, among others, building new or expanded networks and supporting dedicated research.

SO4: Increased capacity and skills of RD stakeholders to optimize research to healthcare continuum

ERDERA will incorporate capacity building activities as integral part of the rare disease research pipeline to enable upgrading of scientific, technology but also regulatory knowledge of stakeholders participating in research projects financed through competitive calls but also those performing "in house" research activities as part of the Clinical Research Network. Moreover, new generations of RD researchers will be equipped with state-of-the-art competences. To unlock the access to RD top-level education to all, the Partnership will develop an accredited, comprehensive online education programme taking stock of highly performing pre-existing modules complemented by novel training units.

SO5: Integrated multinational & multi-stakeholder R&I ecosystem for rare diseases

The Partnership will break the silos between communities by consolidating the already existing strong community and stepping-up the integration of underrepresented perspectives, namely the industry, regulatory bodies and payers. Through dedicated onboarding mechanisms, ERDERA will gradually bring in additional players to attract and increase the critical mass of resources, know how, talents and excellence, but also to erase white spots on the RD research map and offer equal opportunities to patients across Europe and beyond. It will catalyse the transfer of good practices to the national and regional level by building or consolidating the RD National Mirror Groups. This will be reflected by relevant governance and advisory structures but also overall Partnership organisation to ensure coherence and maximise impact of all actions.

The Operational Objectives supporting SOs and GOs and to be reached via activities described in Section 3 are: **OO1: Investment in patient need-led research and innovation, OO2: Support robust data, resources and expertise infrastructure, OO3: Coordination and alignment of European, (inter)national and regional research strategies and resources, OO4: Training and education (of RD stakeholders) and OO5: Multi-stakeholder collaboration.**

The linked Key Performance Indicators, and thus their measurability and achievability, of all ERDERA's objectives are specified in the dedicated table of section 2.1. Furthermore, ERDERA (see also Methodology & WP1 Annual Work Plan) will implement performant monitoring system, allowing on traceability, with dedicated means of verification for each type of activity and partnership as whole. This

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will enable collection of data necessary to measure the progress towards, and achievement of Partnership's objectives.

1.1.4 Coherence and synergies to broader policy objectives and priorities set by the Commission, including links with global strategies and agreements such as the Sustainable Development Goals

The objectives of ERDERA have been consciously designed to align with broader policy objectives of relevance to the RD field (as well as complementary domains) as well as to multiple strategic priorities of the European Commission. All GOs complement several of the priority intervention areas for Horizon Europe: not only 'non-communicable and rare diseases', but also 'health throughout the life course,' 'tools, technologies and digital solutions for health and care including personalised medicine' and 'health care systems'. Although the Partnership is first and foremost centred on research, it is acknowledged that a very close collaboration between healthcare and research is necessary. The GOs and SOs are aligned with the priorities of the *Health* Cluster of Horizon Europe: (i) Staying healthy in rapidly changing society (GO1&3, SO1&4); (ii) Tackling diseases and reducing disease burden (GO3, SO3), (iii) Ensuring access to innovative, sustainable and high-quality health care (GO1, SO1), (iv) Unlocking the full potential of new tools, technologies and digital solutions for a health society (SO2) and (v) Maintaining an innovative, sustainable and globally competitive health-related industry (GO2, SO5). The SO2 is aligned with the EU political priority 'a Europe fit for the digital age', the European Digital Strategy (strengthening digital sovereignty and setting standards across this 'Digital Decade') as well as the European Data Strategy, with data-driven innovations bringing better and more personalised medicines and evidence-based policy. GO2 and SO5 will support implementation of the Industrial Strategy and promote the 'economy that works for people. And the stronger Europe in the world'. Furthermore, the Partnership's emphasis on integrating and building capacity in all EU MS and associated countries (SO4, SO5) aligns well with the Horizon Europe component on *'Widening participation and strengthening the European Research Area'*.

RDs are very much a global challenge, thus it is important that this Partnership contributes meaningfully to the UN SDG agenda. Three key SDGs are particularly relevant here: **1. SDG 3 – Good Health and Well-Being** -the Partnership will ensure a 'joined-up' approach, both to stakeholders and also to policies and strategies, in order to contribute to better health and wellbeing, specifically the following components: understanding the burden of RD on patients, families and societies at large; bringing more (and more accurate) diagnoses to patients, faster; enabling the most promising research to result in effective therapeutic or care products patients can access. In this way, the RD Partnership is contributing actively to the goal of giving all patients access to Universal Health Coverage. **2. SDG 9 – Industries, Innovation and Infrastructure:** Advancing research in RD requires collaboration across stakeholder groups as well as geographies, and industry engagement is an essential component. The Partnership will work with industry and industry associations to maximise collaboration in the pre-competitive space, to support more needs-led innovation (through direct support to ATMPs technology advancement, better understanding of the needs of RD populations, through partnership with patients at all stages of research, and by accelerating the translation of innovation into patient benefit). The Partnership will, through engagement with the digital and technology sectors, ensure a strong focus on evolving, refining and implementing resilient data infrastructures to support research and better health, in order to develop and promote the use of high quality, ethical, and regulatory-compliant tools across all sectors of the research ecosystem. **3. SDG 10 – Reduce Inequalities:** Patients living with RD experience multiple inequalities compared to individuals with more common disorders. ERDERA will make a meaningful contribution to addressing this goal, particularly by reducing the uncertainty and anxiety of often-avoidable diagnostic odysseys and increasing the prospects of more (and more effective) therapies in future. It will pool expertise and maximise data usage to find diagnoses for underserved diseases to better know the natural history of RD and more, it will increase the expertise locally & globally to improve clinical care, will open access across Member States to research on interventions and will engage with patients' own priorities to help them maximise their personal potential. By ensuring a focus on connecting the national, European and global levels, and fostering renewed momentum on plans and strategies for RD, it will support greater research-relevant benchmarking, which will illuminate inequalities for often marginalised and vulnerable RD populations whilst also supporting a greater national awareness of the extent of inequalities and needs in the health and social domains, thus enabling actions.

1.1.5 Collaboration with other partnerships and Union programmes

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Even though it involves more than 170 partners, many of which are network-based organisations, ERDERA is part of a larger ecosystem. Thus, to fulfil its missions and ensure constant complementarity, knowledge and resources sharing and optimization, the Partnership will leverage relevant European actions and will conversely generate content that may benefit other EU initiatives. Three main collaborations' targets are envisioned at this stage: (i) Collaboration with European Union Partnerships, (ii) Collaboration with European Union Programmes, Projects and Initiatives, (iii) Collaboration with other large European or international initiatives. Synergies with different types of activities in the Partnership and funding support will be further identified with the aim to support and enhance specific activities, as well as dissemination and exploitation of results. For each collaboration "opportunity topics" refer to the Rare2030 recommendations covering diagnosis, treatment, care, research, data and European and national infrastructures that set out the roadmap for the next decade of rare disease policies and are also applied in the Partnership's SRIA. The complete list of identified initiatives is available in the Annex 1 of the SRIA "European Partnerships, EU Missions, EU Programmes, Projects and Organisations of potential relevance".

EU Partnerships: Key collaboration opportunities have been identified with several **EU partnerships** in three main areas: (i) the Health Cluster (ii) the Digital, Industry and Space Cluster, (iii) partnerships with cross-sectoral themes. Strong collaboration will be initiated with **four EU Health partnerships**: IHI, ERA4Health, Personalised Medicine and Health and Care Systems Transformation. Collaboration is also foreseen with **cross-sectoral partnerships** such as the EIT Health, Innovative SME and EOSC. Finally, to ensure best uptake and alignment in data, computing and machine-learning research areas, **two Partnerships lying under the Digital, Industry and Space Cluster** have been identified as potential candidate for partnerships, the EuroHPC and the AI, data and robotics partnership.

EU Programmes and Initiatives: The Partnership will also take advantage of pre-existing and to-be funded EU Programmes and EU projects to maximise the use of resources and alignment. It will build synergies with Horizon Europe initiatives (such as European Innovation Council - EIC, or Cancer Mission) or programmes (EU4Health Programme and the Digital Europe Programme - DEP). The ESF+ (European Social Fund Plus, invest in education, employment and social inclusion), InvestEU and ERDF (European Regional Development Fund) will be systematically considered to develop, upgrade and uptake the outputs of ERDERA activities.

Other European and international programmes and Initiatives: In addition to the above, collaboration and/or interaction will be developed (whenever pertinent) with overarching European or international major initiatives of which a first tentative list is included in the Annex 1 of the SRIA.

1.1.6 Transitioning from research to value enhancement: the exit strategy #§PRJ-OBJ-PO§#

The ERDERA is a large research Partnership that will reach its ambition through on the one hand *developing* novel research, tools, and services useful to the rare disease community. And one the other hand through *delivering* that research, tools and services to public and private organisations including funding organisations and companies in a way that fits their business model and value proposition allowing them to seamlessly incorporate the research, tools and services into their day-to-day operations. However, lessons learned from ERDERA's predecessor EJP RD indicate that research institutions and grant funding with limited timeframe are great for *developing* novel solutions but not necessarily for *delivering* them to end-users through a fit with end-users' business models and their practical reality. Furthermore, ERDERA's output must not only be relevant for public and private stakeholders (including funders and companies) as end-users, but also make attractive to the public and private funders and research organisations to share their data with ERDERA as part of developing an attractive data infrastructure that can be explored by end-users in the delivery phase. This calls for an exit strategy where the grant provided for the development phase will in fact be equivalent to an investment as the return is reaped in the delivery phase. Hence, from its inception, ERDERA will work on an exit strategy aimed at achieving long-term sustainability linking development with delivery. It will begin with defining the vision of the sustainable ERDERA, then proceeding to operationalise it by identifying its core value components such as infrastructure for data and expertise, clinical research services and research funding support and finally creating the necessary incentives for knowledge sharing, fostering a commercial mindset and deciding on legal entity and governance structure. Building upon insights gained from the EJP RD Sustainability Report, the Partnership will work towards the establishment of the European (Federated) Rare Disease Institute (RDI), equipped with the operational capacity to deliver value that can garner long-term commitments and financial support from public and private organisations including funding organisations and companies. During the first 4 years of the Partnership, the focus will be on developing the business case of the European Rare Disease Institute. During the remaining 3+3 years ERDERA will work together with key stakeholders, including Member States and the European Commission, to develop a political support for the delivery and exit strategy to finally conclude the creation of the legal entity for the institute.

#§PRJ-OBJ-PO§#

1.2. Methodology #@CON-MET-CM@# #@COM-PLE-CP@#

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To support its ambition and missions, the European Rare Diseases Research Alliance (ERDERA) has been designed as a comprehensive and integrated ecosystem accelerating research and innovation in the field of Rare Diseases (RD). In simple words, its structure can be compared to an *institute* encompassing three main parts: (i) **funding,** (ii) **internal (in house) Clinical Research Network** that implements research activities targeting clinical trial readiness of RDs and accelerating diagnosis and translation of research discovery into improved patient care, and (iii) **related supporting services** that serve external and internal RD community. The three blocks are composed of several interconnected Work Streams (*departments)*, each focusing on a specific aspect of RD research and innovation, and supported by all-embracing **coordination and strategy** and foundational **(inter)national alignment.** It is important to underline that despite not being a "material" structure, the federated nature of ERDERA takes advantage of well-established elements (e.g. multinational RD funding, ERNs, supporting services pressure tested by EJP RD, Virtual Platform of data, strong patient organisations) that are combined with new, missing or underdeveloped building blocks (e.g. ATMPs technology & innovation, federated diagnostic pipeline, European-scale RD education programme, public-private undertaking), and jointly form a unique infrastructure, tailored to the needs of RD community and supported by solid governance and strategy. By bringing all components and stakeholders on board ERDERA can tackle system-wide scientific and operational challenges that no one institution can overcome individually.

The overarching **Coordination** is vital for ERDERA's daily operations and sustainability as it will involve activities essential for maintaining cohesion, alignment, and synergies across the ecosystem. It entails a comprehensive system of actions and processes encompassing governance & strategic prioritisation, patient involvement, continuous monitoring, intellectual property rights, data-driven decision-making, ethical compliance, and communication & dissemination.

The **Governance & Strategy** of ERDERA involves several core bodies (Governing Board [GB], Board of Funder [BoF] and Multistakeholder Advisory Board [MAB]) that are closely connected and informed by executive level. The Coordination team, led by INSERM, provides the necessary tools, documents, and agendas, and works closely with the Monitoring Task leaders to provide regular updates on the partnership's performance or policy analyses. The GB and MAB will meet regularly to discuss strategic and policy matters and approve the Annual Work Plans of ERDERA. The MAB, composed of 20-25 independent key opinion leaders, can initiate Thematic Groups, and thus enlarge, whenever needed, its expertise to address topics of interest brought by ERDERA partners or GB. The final decisions on funding opportunities are driven by the BoF. To ensure that ERDERA's activities are led by patients' needs and aim to improve patient outcomes, **Patients & Public Involvement and Engagement (PPIE)** is embedded at all levels through the coordination of EURORDIS and the support of various patient organizations constituting the core PPIE group. Based on a PPIE framework, the group will support all involved patients and representatives, advise and provide feedback to ERDERA's executives, help in identifying patients for research tasks, monitor engagement, link activities to Education & Training, and develop resources for patients and families. To monitor timely delivery of foreseen outputs, risk strategy, required investment and reallocation of resources, advancement on the pathway to impact, an **exhaustive monitoring system** has been designed to serve the coordination and enable data-driven decision-making. The challenges of IPR management, ethical compliance, and long-term sustainability will be dealt with by entering into a Consortium Agreement, setting up an Ethics Advisory Group, defining a structured vision of the ERDERA legal entity, mapping relevant business models and legal settings, and considering costs and financing aspects. To build and maintain the support of RD community and other non-RD stakeholders, and to ensure the exploitation of the generated results and services the ERDERA's strategy for **communication and dissemination** will be designed, observing Open Science principles, and tailoring to specific audience groups' needs. Synergies with Work Streams will be leveraged to develop ERDERA branding and communication materials, supporting the partnership in their communication needs. Together, these activities will contribute to creating an all-inclusive, supportive, well-organized, and efficient environment necessary for ERDERA's day-to-day operations and long-term sustainability.

1.2.1 ERDERA's building blocks

The Rare Diseases Funding workstream **(WP3-5)** is a paramount part of the ERDERA and engages various and complementary stakeholders such as funding agencies, private sector organizations and philanthropic foundations. It creates and implements tailored, competitive funding programmes (joint transnational **[WP3]** and clinical trials calls **[WP4])** leveraging national and EC commitments (over 167

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M€ committed by participating countries; around 30M€ of EC budget solely dedicated to support Clinical Trials). All funding opportunities aim to foster patient-centric, transnational, multi-stakeholder research projects. To respond at the best to the needs of RD community, and encompass any new emerging needs, the selection of topics of the calls is based on gap analysis combined with strategic and policy recommendations from the ERDERA's advisory and governing bodies and, whenever relevant, public consultation. To ensure patients are equal partners in research, specific budgets are dedicated to funding patient advocacy organizations (PAOs) involved in research projects. By integrating the support in translational mentoring, regulatory aspects, and FAIR data management during the application process, along with targeted training opportunities, ERDERA ensures efficient execution and increased innovation of all funded projects. Finally, to enhance knowledge sharing of pre-existing collaborations and to spark building of new research networks for underserved rare diseases or undiagnosed patients, the Partnership will continue **the Networking Support Scheme (NSS, WP5)** established under EJP RD as proven instrument to empower people living with rare diseases, involve stakeholders from widening countries, engage young researchers, and strengthening collaborations with national and international stakeholders.

The Clinical Research Network workstream **(WP6-12)** is the second arm of the Partnership that, through the in-house research activities, aims at developing and demonstrating scientific and operational innovations that accelerate diagnosis, improve clinical trial readiness, aid in evaluation of RDs burden and support development of innovative therapies. Empowered by the expertise and capacity of the European Reference Networks and other relevant clinical centres, similarly to the Funding work stream, the CRN is closely interconnected to all supporting services (see below). To deliver on ERDERAs objectives, the R&I activity of the CRN is organised around three main domains: **diagnostics, clinical outcome, and advanced therapies research**.

Decreasing time to diagnosis from 4 years to 6 months after coming to medical attention for every RD patient is a high-level goal that requires significant scientific and structural efforts. This involves, among others, innovative diagnostic research strategies, enabling access to the newest technologies, and transferring generated research standards to diagnostic centres to close the gap between research and healthcare. The CRN's Diagnostics Pole will tackle this by **building** (diagnostic) **research data availability on a European scale (WP6),** while coordinating **genomics diagnostic research pipeline (WP7).** To up-scale and consolidate a secure environment to share data on undiagnosed RD patients for ERNs, Undiagnosed Disease Networks (UDNs) and diagnostic centres, WP6 will use the proven collaborative Solve-RD infrastructure model and implement a **federated approach** leveraging on national 1+MG/GDI infrastructural elements**.** It will involve national undiagnosed rare disease programs (UDP), national diagnostic centres (including in underrepresented countries), and the ERDERA's Data Services Hub. A Data Availability Committee will be established to ensure the quality and integrity of the diagnostic data, compliance with ethical considerations and responsible data usage, through monitoring of the data sharing. The centrally or locally collected data of undiagnosed cases will be re-analysed thanks to the unique combination of clinical expertise of ERN members and state-of-the-art knowledge of data scientists jointly organised in working groups. Whenever relevant, **innovative genomics methods and interpretation approaches (WP8)** like long-read sequencing (LRS) platforms, optical genome mapping, and multi-omics analyses to detect missed or hidden variants and gene regulatory aberrations will be used. Any generated new methodologies, guidelines and research results will be disseminated via publications and international databases to enhance global uptake. Efforts will be made to monitor and continuously improve the time spent at every step of the diagnostic chain, and all pipelines and software developed will be released. It is expected that the combined efforts of WP6-8 will provide a complete and generalizable workflow for all RD patients thus significantly accelerating RD diagnoses.

To design clinical trials and evaluate potentially transformative treatments, researchers, biopharmaceutical companies, and regulators need high quality, natural history data, as well as biological and clinical outcome measures fit for the intended purpose. The absence of such information represents a major bottleneck in therapy development for many rare diseases. Thus, *Clinical trial readiness* can be understood as *the state of having validated clinical research tools and knowledge of disease natural history necessary for the design of efficient clinical trials.* To accelerate clinical trial readiness of RDs the **WP9 and WP10** constitute the so-called Clinical Outcome Research Pole of the CRN. More specifically, **WP9** aims to process real-world RD cohort data for clinical trial readiness. It will develop generalizable solutions through specific case studies selected based on thematic complementarity, feasibility, data readiness and relevance for

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therapeutics development. Both structured and unstructured Electronic Health Records (EHR) data will be processed with the help of Natural Language Processing experts and Data Service Hub specialists. Innovative strategies for population-based outcome research will be formulated, with an emphasis on crafting guidelines to produce FAIR-compliant population datasets. The **aim is to create a universally applicable, interoperable dataset anchored on linked European Reference Network (ERN) registry and social security data**. The advantages of merging existing RD patient cohort data will be highlighted with the objective to craft robust reference groups, poised to serve as benchmarks for upcoming clinical trials. Procedures for academia-driven patient **registries and natural history studies** will be established during the sequential stages of engagement with regulatory authorities with the goal of securing EMA **qualification for regulatory-grade natural history registry data for potential utilization as external comparator arms in non-randomized clinical trials** in rare diseases. Additionally, these procedures are designed to **assist in post-authorisation safety surveillance (PASS) and efficacy (PAES) studies**. Existing model-building technology will be utilized, and new methodology will be developed to create Drug Development Tools (DDTs) to **enhance the comprehension of RD progression patterns and facilitate quicker and cost-effective predictions regarding the effectiveness and safety of new therapeutic products**. The C-PATH Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP®) will be leveraged as a central, standardized infrastructure to support and accelerate rare disease characterization. Additional expertise in operational and regulatory aspects will be sourced from WP 14 and 18.

WP10 brings multidisciplinary expertise to address the key challenges of patient-centred outcome research in RDs. It **focuses on the promotion of implementation of Patient-Cantered Outcome Measures (PCOMs)/Patient-Reported Outcome Measures (PROMs) in RD** contexts, which is hampered by the insufficient number of validated tools developed for RDs. The ERICA consortium has generated a PCOMs/PROMs repository of validated tools in RDs, which will be linked to functions and disabilities in the WHO International Classification of Functioning, Disability and Health framework for measuring health and disability at both individual and population levels. This will **facilitate the process of PROM scale generation and improve patient care pathways, health status monitoring, clinical therapy guidance, and health outcomes**. Data standardization and efficient, regulatory-grade data capture are required to leverage the full power of these PCOMs/PROMs datasets. They will be integrated with other Clinical Outcome Assessment tools and biomarkers via interaction with WP9, paving the way for personalized medicine in RDs. The overall process from regulatory and ethical PCOMs/PROMs clearance management to data integration and analysis through Machine-Learning approaches will be designed and validated through four use cases involving the collection of patient-generated data using mobile health solutions and devices thus demonstrating the capacity of ERDERA to improved comprehensive knowledge framework integrating the EU, national/regional data and information infrastructures to improve translational research, clinical trial readiness, and impact of RDs.

The **WP11 and WP12,** the Advanced Therapies Pole of the CRN, are critical to **accelerate the development of new therapies**, especially for RDs remaining without any therapeutic options. WP11 will expedite the clinical translation of Advanced Therapeutic Medicinal Products (ATMPs) developed in WP21 (Technology Accelerator, see below) by creating a comprehensive collection of procedures and methods that will help in identifying rare diseases, matching them with suitable technologies, and simplifying the procedures to access clinical trials. Clinical, technological and patient experts will agree on diseases to be prioritized and match them with the most advanced and suitable technologies in the Tech Accelerator Hub. The subsequent work will focus on performance testing of these technology platforms in proof-of-concept studies to demonstrate their application in translating research for ATMPs development and their final procurement as service to ATMPs developers.

Further to the above, and to support solutions for patients with ultra-rare diseases that remain outside of scope for more traditional drug development business models, ERDERA will address the **development of individualized antisense oligonucleotides (ASOs) within an academic and named patient setting**, without the intention of marketing authorization **(WP12)**. This approach offers more flexibility and represents a significant paradigm shift. To that end, a new platform, based on *hub and spoke model* will be created to ensure the safety, standardization, and timely development of individualized treatments. The platform will be supported by a board consisting of a multidisciplinary group of experts, including patient groups, clinicians, researchers, and ethicists, to discuss patient eligibility, select appropriate outcome

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measures, and ensure equity in the selection of the most eligible patients. The platform *hub* will be responsible for patient identification process, ASO design and synthesis, safety assessment in cells and animals and ethics. On the other hand, the sites treating patients with individualized therapies (*spoke*) will oversee measurement of relevant outcomes, design of the study/treatment regimen, local regulatory aspects, and challenges for local treatment implementation. The platform will be tested using four use cases and subsequently rolled out to other partners. The work performed under Diagnostics Pole of the CRN (WP7-8) will identify additional patients with mutations eligible for individualized ASO treatment. Patients will be treated in a named patient setting, but to facilitate drawing of transferable outputs, the coordination with methodological experts of WP 19 will allow assessing efficacy of the platform approach across diseases and treatments. In addition, the treatment response will be captured in a specific registry, built with the support of Data Service Hub, enabling individualization for each patient, and ensuring interoperability with other patients' registries at the same time. WP11 will draw on already existing first emergent cross-European networking efforts initiated by the two task leaders, (LUMC, UT), both coordinators of "1 mutation 1 medicine (1M1M)", including first contacts to underrepresented countries (via ERN-RND and linking to WP24). Tight interaction between WP11 & 12 and with other work packages, especially the PPP collaboration Accelerator (WP22) will be crucial to identify a common and efficient strategy for initiating clinical studies for innovative therapies in rare diseases. In this regard, a clinical trial application of the validated ATMP(s) will be prepared at M84.

Support services: Data, Expertise, Education & Training and Acceleration Hubs

To ensure efficient execution and maximise transability of results and innovation of research activities (encompassing CRN and all funded projects) a comprehensive suite of support services is at the heart of ERDERA.

The Data Services Hub (DSH) is developed to **facilitate data capture, integration, analysis and sharing** across the RD community. It comprises a proper **Data Hub** (composed of an integrated network of FAIR data sources, analysis methods, knowledge bases, and computing components created collaboratively by all partners in ERDERA) and associated **services** supporting FAIR data processing by ERDERA research activities (funded and in-house) and, with the data-driven monitoring system, informed decision-making. Together Data Hub and Services will **enhance the value of rare disease data and knowledge on a global scale,** thereby increasing research capabilities and efficiency for a wide range of stakeholders, including patient organizations, industrial partners, policy makers, and researchers. The DSH will also interact with other data infrastructures and initiatives (such as Euro HPC, 1+MG/GDI, GA4GH) to stimulate DSH developments and provide reusable solutions. The EJP RD has already developed a federated infrastructure for RDs research data, known as the Virtual Platform (VP). Today the VP comprises catalogues of resources, registries, biobanks, knowledge bases and tools compliant with agreed standards (https://vp.ejprarediseases.org). **The WP13** of the DSH (in close collaboration with WP14-16) will **scale up the VP** by integrating case studies from the Clinical Research Network (CRN) and Joint Transnational Call (JTC) funded projects, **triggering the development or refinement of existing services and tools for future reuse**. Being designed as a virtuous cycle that can be triggered at any stage and by any ERDERA case study or project, the DSH will ensure integration, compliance, and findability of the outputs in the VP. Specifically, **WP14** will provide methodologies and tools **for data capture.** It will enable, on one hand, the resources to describe their data and exchange formats, Application Programming Interfaces (APIs), access permissions, and analysis capabilities using ontology-based machine-actionable models allowing automation agents to read this information and perform appropriate actions. On the other hand, it will develop data ingestion services leveraging on RD projects like EJP RD and Solve-RD.

WP15 will provide methods, tools, and infrastructure **for data deposition, sharing, and analysis**. It aims to sustain and adapt resources for large-scale collaborative data analysis, focusing on implementing portable pipelines enabling federated multi-centre analysis, and developing the necessary infrastructure for secure processing environments. To that end, ERDERA will strive to use EU capacities such as those from the Euro-HPC Joint Undertaking, another Partnership under Horizon Europe, by following available standardised application process and discussing collaboration models to improve EU cooperation and capacities on health data in general. Scaling up of patient sample size, coupled to environment respecting legal and ethical considerations, will facilitate coordinated queries and analyses. Such federated learning will be directly used to discover gene-disease associations and identify modifiers in molecularly diagnosed cases. To **accelerate the innovation of knowledge modelling and exploitation** the DHS will develop and

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integrate pre-existing knowledge resources around **Rare Diseases maps (WP16).** For this purpose, it will create and align knowledge bases and ontologies needed for PCOMs/PROMs, antenatal phenotypes, and rare disease (bioinformatic) networks. Designed to scale with the number of projects funded through JTCs and the CRN, it will provide them with applications for data annotation, genetic variant analysis, molecular pathway & networks to investigate undiagnosed cases, molecular causes of how treatment works and compare with existing treatments and innovative RD research. Ultimately, the **DSH will provide standardized and scalable methods, tools, and services embedded in a data ecosystem**.

The Expertise Services Hub (ESH) will provide **know-how and support on specific aspect of translational research and clinical studies** to all ERDERA partners and all funded projects. It is recognized that the translation process is long, complex, and requires strategic planning, as it involves multiple disciplines beyond science, such as regulatory science, health technology assessment (HTA), data and innovation management. Most of the time such knowledge is not instantly available to research teams, thus likely impacting the expected outputs and their relevance. The ESH **WP17 will focus on mentoring in the translational research process**, which is crucial for the effective development of knowledge from biological discovery to application level, and vice versa. To address this, the pool of mentors will be available to the research teams, applying to JTCs and CT calls, from the application stage (full proposal). Mentors will guide the project team through the expected and predicted translational bottlenecks and help in identifying specific gaps that may require adjustment of the proposal content and, eventually, additional expertise. This shepherding support will continue once the projects are financed. Furthermore, to assess the potential need for additional more extensive support based on a *consultancy* model, a feasibility study will be conducted and informed by user experience and mentors' feedback. It will also help in defining a potential business model for the long-term sustainability of the service.

Regulatory science is vital for ensuring that scientific research and its resulting products and technologies are safe, effective, ethical, and environmentally friendly, thereby promoting innovation, building public trust, and facilitating marketing of products. Thus, regulatory support must be integrated as part of the R&D process. ERDERA's **WP18 will provide regulatory support through a dedicated group of regulatory experts from various sectors** including industry, academia, not-for-profit organizations, patient representatives, and public sector. The establishment of an effective monitoring, assessment, and support process, which is conducted in close collaboration with other WPs, will be central to this service to ensure that all regulatory needs are prioritized and adequately supported. The Regulatory Support Group will be responsible for providing relevant expertise, guidance, and recommendations. Regular liaison with the Ethics Advisory Group will be maintained to ensure alignment on ethical and regulatory strategies and to jointly address requests for support. Overall, this support service will play a crucial role in navigating the complex regulatory landscape, ensuring ethical alignment, and providing ongoing support to all stakeholders involved in the translational and clinical research and processes.

In the context of rare diseases, the available information per subject is substantial (often linked with patient diagnostic journey), but the number of subjects is typically small, which leads to complex, multivariate data that may include outcomes of different data types, measures taken longitudinally, hierarchies in the data, and general incompleteness. Therefore, it is crucial to apply methodology that is statistically adequate (precise and unbiased) and computationally feasible, while ensuring proper integration of clinical trial and Real-World Data, such as epidemiological studies and registry data. The **WP19 will provide Clinical Trials/Studies methodological support**, building on the collaborative tradition of IdeAL, ASTERIX, InSPiRe[19] [1], and the EJP RD[20]. Various methods, including likelihood and Bayesian methodology, randomization-based methods, and methods based on generalized pairwise comparisons, will be considered. The expertise will be provided directly to research teams and liaison with the Regulatory Support Group will be established to discuss the possibility of undertaking the EMA Qualification Procedures for the innovative methodologies to be developed, in order to further enhance their efficient transfer to the clinical field (i.e., to the Clinical Research Networks and other centres throughout the EU where clinical trials and other empirical studies are conducted).

Education and training in rare diseases research

[19] https://tinyurl.com/mrdms2nw

[20] https://www.ejprarediseases.org/funded-projects-demonstration/; https://www.ejprarediseases.org/funded-projects-internal-call-for-innovation-project-in-clinical-trials-methodology/

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The Education and Training is crucial for building and sustaining the capacity of the RD research and innovation community. Important gaps remain, and novel needs must be continuously monitored and addressed across multiple dimensions including career stages, multistakeholder community, geographical regions and research and innovation developments. ERDERA, is strategically positioned to address these needs by acting as a direct provider, major contributor, and collaborator in education and training activities, as well as an advisor for education-related policy and decision-making. The **Education and Training workstream proposes dedicated program that is comprehensive and targets general overarching needs in RD research, with a focus on highly specialized and intermediary levels of expertise**. It is organized thematically to empower multistakeholder communities, including patients, young researchers, and professionals involved in RD diagnostic research, research methodologies, translation of research, clinical research and data science. A blend of online and face-to-face training courses, as well as the implementation of an interuniversity European diploma, are part of ERDERA's operational approach to building capacities. Key components include the engagement of international multistakeholder faculties, wide geographical coverage of trainings, a gradual and scaled approach to trainings according to the learner's level of expertise, development of open and shareable educational resources, and application of the train-the-trainer principle. ERDERA also focuses on increasing participation of underserved groups and learners from underrepresented countries by offering fellowships for training courses and implementing specific measures in other ERDERA workstreams. The program involves various education and training providers, including universities, medical and nursing schools, professional organizations, ERNs, patient organizations, and research performing organisations. It encompasses diagnosis, integrated and coordinated care, patient empowerment, and research themes, while avoiding duplication of efforts and sharing responsibilities among all providers. This workstream will not only empower the current generation of researchers, clinicians, and other professionals involved in RD research but will also nurture the next generation of experts.

The ERDERA's **Acceleration Hub** is designed to translate scientific findings in the biomedical domain into socio-economic value. The average cost of getting a new medicine into marketing authorization exceeds USD 2 billion[21] [3],[4], making early translation particularly difficult. This stage, known as the 'Valley of Death,' is crucial for academia and non-profit organizations to undertake given the challenging market conditions for industrial development in rare diseases (RD). Thus, academia and their funders play an important role in RD innovation by 'de-risking' projects, building a strong knowledge dossier about the target, disease, and intervention so that commercial and other stakeholders would invest in the costly clinical development pathway and implementation into the healthcare domain. ERDERA aims to create an **accelerator framework** to address above-mentioned challenges by leveraging public and private expertise in disease biology and technology development, as well as clinical expertise available in the CRN. Specifically, **the Technology Accelerator (WP21)** focuses on **streamlining promising gene transfer technologies**, including in vivo delivery of recombinant nucleic acids using adeno-associated virus (AAV)-derived vectors, messenger RNA (mRNA), and delivery systems such as lipid nanoparticles and extracellular vesicles. These delivery systems can be used for newly developed gene editing technologies aimed at curing the cell's genome through in vivo or ex vivo strategies. WP21 will address improved manufacturing processes, analytical characterization, demonstration of clinical utility, and evaluation of therapy response and immunogenicity issues related to in vivo administration of ATMPs. The addressed tools, methods, and protocols will receive continuous advice, monitoring and assessment mechanisms from the Expertise Service Hub. The most promising technological strategies/platforms will be further explored in WP11, in alignment with the prioritized diseases. Outputs of WP21 will also be considered for the selection of case studies in WP12, and to support possible applications to JTCs fostering therapy development topics in years 4-7. A strong involvement of industry partners, each providing significant in-kind resources and expertise for the technical development tasks, will ensure rigorous development planning and timely engagement of regulators, so that outputs are qualified in the context of use. By creating systemic and open access solutions, the Technology Accelerator aims to broaden EU innovation capacity and increase the number of projects entering clinical development.

To complement ATMPs technological developments and to streamline the advancement of other promising early-stage diagnostic or therapeutic interventions by leveraging on **Public-private Collaboration**

[21] https://tinyurl.com/yjmrectb, https://tinyurl.com/2z423yds

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acceleration, the **WP22** will create an innovation marketplace. This marketplace will connect promising RD projects with R&D experts, patients, and public and private investors to enable further development and clinical implementation. Selection criteria, workflows, and legal documentation to identify, evaluate, and select projects confidentially will be developed. The PPP Collaboration Accelerator will also engage third-party investors and innovation funders (ranging from non-profit research funding philanthropies and charities to corporate and independent venture capital as well as national and EC innovation funding vehicles such as European Innovation Council and Eureka), leveraging on the proven concept of the FFRD Proof-Of-Concept Club, to create a vibrant group of funders willing to commit resources to selected projects. Selected projects will be supported to become investment-ready through business planning, coaching, and non-clinical development also in collaboration with other relevant synergistic initiatives like REMEDi4ALL (drug repurposing), EU PEARL (advanced trial design/platform trials), RD Moonshot or IHI projects supporting RD. The goal is to secure a path to clinical implementation for each project, either through commercialization via out-licensing, collaborative development, or a non-commercial implementation strategy.

The **(Inter)national Capacity Alignment** workstream is a foundational block of ERDERA that fosters **the coherence and contribution of the national/local and international RD research activities and resources** with the Partnership and within the overall RD ecosystem. It will also watch over the already pooled national resources committed through the letters of intent of ERDERA's partners from 28 EU countries. To that end **WP23 aims to develop and promote the so-called National Mirror Groups (NMGs)** that will be at the heart of national activities and RD strategy by bringing relevant stakeholders, facilitating interactions, collecting comparable information on national RD activities, and generating new knowledge to optimize synergies for greater alignment. The outputs of NMGs will be shared to adapt EREDERA's activities by addressing National RD research needs. In return, ERDERA's services and results will be promoted at the national and local levels.

WP24 focuses on the engagement of underrepresented countries by identifying specific requirements and expectations, assessing conditions and barriers, establishing synergies, undertaking advocacy and awareness-raising actions, and developing guidelines and programmes. This will encompass mapping exercises, RD research activity assessments, knowledge exchange, cooperation with relevant identified entities, benchmarking, and analysing existing measures and guidelines. Finally, **WP25 will amplify the impact and effectiveness of global collaborative efforts and drive transformative change at international scale** by aligning the research strategy of the ERNs, engaging with IRDiRC and supporting its scientific secretariat, establishing international strategic alliances and organizing joint workshops and conferences with Clinical Research Networks from all over the world. Continuous liaison with all ERDERA workstreams will be ensured to align and synergize efforts, with a particular focus on the RD research funding, the Clinical Research Network, and the Education and Training in RD Research.

1.2.2 Social sciences and humanities: People with rare diseases often experience unique challenges, including delayed diagnosis, limited treatment options, and social isolation. Aiming to contribute to the General Objective 3 "better understanding of the impact of RD on patients, families and society", ERDERA will help in understanding the psychological, social, and cultural impacts of living with a rare disease for the development of better support systems and interventions that address the specific needs of individuals and their families. The interdisciplinary approach will combine medical, genetic, and biological research with insights from Social Sciences and Humanities (SSH). This approach will lead to a more holistic understanding of rare diseases and the development of comprehensive solutions.

The PPIE Patient and Public Involvement & Engagement group, formed from representatives of participating patient organizations, will ensure that all activities are led by patients' needs. The JTCs will cover topics of interest for patients including human and social sciences and interdisciplinary research, leveraging on the experience gained from the EJP RD JTC 2021[20]. The NSS will foster support to events involving PLWRD and fund opportunities addressing SSH challenges and knowledge sharing. Moreover, the outcome research activities of the CRN (particularly WP10) are anchored in SSH field through the PCOMs research that enables person-centred health and social care[22], and the estimation of the socioeconomic impact of RDs in Europe based on real-world data and disease modelling approaches. Additionally, a team of economists is included as an integral part of the WP1. Leveraging expertise from economic and business sciences will be instrumental in shaping and implementing exit strategy from the ERDERA's inception to its conclusion and beyond. Drawing from the economic theory and literature, this

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team will seek to design the most suitable incentives for long-term commitment and value creation. Furthermore, the ethics management activities (as part of the Humanities) will contribute to providing a framework for decision-making that considers the rights, values, and preferences of all stakeholders for addressing issues and dilemmas around use of experimental treatments, access to limited resources, and participation in clinical trials. Finally, the PPIE group and the communication team, as well as the ERDERA multistakeholder trainings, will enable effective communication between patients, healthcare providers, and researchers. Along with the NMGs action, they will help in understanding and considering the cultural factors that can influence the perception, experience, and management of rare diseases, supporting a culturally sensitive interventions and support systems.

1.2.3 Gender Dimension: The World Health Organization noted that gender inequalities hinder access to healthcare, a situation exacerbated by the rarity, complexity, and severity of Rare Diseases (RDs)[23]. Moreover, there is a documented gender bias in RDs healthcare, with women typically being diagnosed and treated later than men, leading to accelerated disease progression, and impacting quality of life, socioeconomic status, and mental health. Additionally, women predominantly undertake informal care tasks for relatives with RDs, leading to increased unemployment, vulnerability, and social exclusion. ERDERA addresses these issues by considering biological characteristics (age and genetic background/sex) and social/cultural factors (gender) in its approach. Inclusion of sex, gender, and diversity as part of research approach will be crucial to obtain access to ERDERA funds. This will be reflected in calls for funding opportunities, proposal evaluations, funded project and in-house activities monitoring, assessment and reporting. ERDERA will ensure communication, dissemination and exploitation activities include all dimensions, particularly when the patient and/or carers' perspectives are sought, by using neutral language; selecting inclusive visual materials representing the whole range of gender/sex and underrepresented population; prioritizing women's participation in all the dissemination, communication, advisory boards and training actions; and monitoring the above-mentioned aspects during ERDERA execution. All the partners are committed to equal opportunities in team composition and will continuously assess all dimensions to identify any other areas with potential gendered impacts.

1.2.4 Open Science: Implementing Open Science practices as a standard for pre-competitive research activities will advance science while preserving commercial potential to incentivize further innovation in RD research and other connected R&I, as part of the ERDERA's IP management strategy. Partners will formally agree on the review of Open Science processes and methodology from the start and through provisions of the Consortium Agreement. It is important to note that business stakeholders, who are important players in the ERDERA, may be deterred from participating in the innovation process if there is no IP protection to safeguard their investments and market position. Therefore, new knowledge generated from translation and applied research should be IP protected to maintain commercialization potential, while supporting early-stage fundamental discoveries that should be open access to advance science. ERDERA aims to establish an Open Innovation ecosystem that aligns with the EC's Responsible Research & Innovation goals[24]. After securing essential IP rights/interests, ERDERA outputs will be made available through open access and following the *"as open as possible as closed as (strictly) necessary"* principles. A preliminary list of deliverables suitable for public distribution is presented in table 3.1c. Whenever possible, the publication on the Open Research Europe platform will be supported, and for field-relevant journals any paywall restrictions will be avoided thanks to publishing routes (green, gold, or diamond). Publications, including newly developed methods protocols, will be shared at an early stage through pre-print repositories (e.g., BioRxiv) to allow transparent feedback before journal submission. Relevant high-visibility journals will be selected. Publications will be shared, promoted, and advertised on the ERDERA website, but also through relevant social media channels to encourage future citations and global visibility of ERDERA. To prioritize transparent disclosure and availability of data, processes, materials, and methods for use and replication by the wider research community the Zenodo open repository as well as other focused directories will be utilized. Relevant scripts and codes generated will be published on GitHub to promote systematic sharing and collaboration and facilitate the application of newly developed computational methods across partners. Once fully developed, these scripts and codes will be made publicly available and, where applicable, compiled into open-source software for bioinformatics, such as Bioconductor. Other open science practices, such as early and open sharing of research negative outcomes, and preregistration, will be evaluated in the context of establishing an IP management strategy (see section 2.2.c Management of Intellectual Property) in close collaboration with the WP2 to maximize ERDERA's impact.

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1.2.5 Data Management Plan: ERDERA will collect and work with a variety of data types. It will develop a sustainable Data Management Plan (DMP), with the support of the Data Services Hub and the Expertise Services Hub, within the first six months of the project to ensure the accountability and reliability of the data, which considers appropriate IP protection and is compliant with ethical rules, standards of research integrity, FAIR principles and GDPR. When finalized, it will be reviewed and agreed by all Beneficiaries followed by formal signature. It will be constantly updated, and the resulting version will be submitted at each reporting period. The DMP will cover the following aspects: i) handling of research data (and other outputs) during and after the project; ii) types of data to be collected; iii) application of data methodology and standards with inputs from the stream "Data services Hub"; iv) mode of sharing and accessing data; and v) data curation and preservation. The DMP will outline the project's scientific, technical and organizational details for data and metadata collection, storage, retention, accessibility, privacy, confidentiality, destruction, quality assurance, backup, and resource allocation. The DMP will comply with all relevant national and EU laws for the protection of personal data, and confirmation of compliance will be requested to all the ERDERA partner organizations including the ones of the funded projects. The DMP will also include permissions to collect, use, reuse, and merge data from relevant authorities or primary owners/data controllers for relevant activities such as the ones of the CRN. ERDERA will employ the Data Stewardship Wizard (DSW) to develop the DMP as recommended planning tool by the Horizon Europe Program Guide. DSW allows assessment of the level of FAIRness of the research DMP, which will enable ERDERA to continuously improve its handling of data throughout the partnership's duration, provide guidance to external users, and enhance the reproducibility of research results. These improvements are essential for successful collaborations with all the partners and effective management of intellectual property. The data generated will be subject to ethical and data protection regulations, and efforts will be made towards full digitalization of the research activities, including the use of standardized digital tools for the definition of workflows and procedures for wide sharing and usability of research outputs across the consortium. To ensure explicit provenance and reproducibility, supporting metadata will accompany all records. Enriching the metadata with open ontologies to optimize data interoperability will be considered. Where needed, electronic data/metadata will be stored on the ERDERA Data Hub and on the collaborative platform (Microsoft 365 with EU servers) for collaborative purposes, secure distribution, tracking of progress and deliverables, and identification of IP potential. Privacy by design and procedures to mitigate potential reverse engineering and unforeseen disclosure will also be covered in the DMP. The whole data architecture will be subject to risk assessment to guarantee security, ethics, and privacy. This will ensure that the data collected is properly processed and managed, with the help of appropriate safeguards and measures in compliance with ethical standards and GDPR regulations. Public content such as public deliverables, workshops, training/info sessions, scientific meetings, and brokerage events will be shared openly on the ERDERA website. Finally, to design a DMP adaptable to a growing degree of data complexity ERDERA will leverage on partners' experience in projects with similar DMP demands, particularly those involved in the Data services Hub and the Acceleration Hub workstreams, contributing to the open science agenda of the EC and publishing FAIR Research Infrastructure data resources; making tools and workflows interoperable and reusable and setting policies, specifications and tools for the management of data for scientific research. The ERDERA DMP will be a dynamic document, updated regularly, incorporating inputs and evolution from the engaged partners and the RD community.

1.2.6 Artificial Intelligence (AI) will be employed in several ERDERA activities including data integration (WP14) and analysis (WP15), serving for large-scale analyses including both genomics and multiomics as well as for high-performance computing pipelines (WP6, 8 & 15). It will also be used for Drug Development processes, including disease prioritization, (WP11), drug formulation (WP21), and clinical trial simulation (WP9). AI also aids in the development of knowledge bases and ontologies (WP16). ERDERA will enable a federated learning infrastructure through AI exploitation (WP15) addressing thus ELSI, GDPR and scalability issues encountered with centralized analysis. As described in the Annual Work Plan Year 1 (AWP Y1), the DSH will develop and/or use AI approaches following requirements for technical & social robustness, accuracy, reproducibility, reliability, and explainability. It will provide quality processes, minimize inaccuracies, validate techniques, and compare the performance of hybrid intelligence to manual approaches. Methods that do not meet these requirements will be discarded criteria (see WP13 methodology in AWP Y1). Additionally, during the development of the AI-based system in the

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technology accelerator, the GAMP5[22] and Quality by Design[23] good practices will be implemented by addressing the above specific requirements all along the development cycle (see WP21 methodology in AWP Y1). All those specifications are considered as Critical Safety Attributes that will be included in the pharmaceutical Quality by Design paradigm of development recommended by the FDA and EMA in the ICH Q8(R2) guidelines. The monitoring of the Ethics compliance task, will support AI developments and implementations to be made socially robust, considering the RD specific context and environment of operation. Whenever they have a significant impact on people living with RD, (such as RD diagnosis & drug development prioritisation) the support will help in making AI systems designed to provide a suitable explanation of their decision-making processes. Importantly, the Expertise Services Hub will support the fulfilment of such requirements, from both the methodological and regulatory perspective. Among others, this latter workstream planned a deliverable that describes the State-of-the art methodology (including AI) that is efficiently transferrable to partners.

[22] Martin, K. C., & Perez, A. (2008). GAMP 5 quality risk management approach. *Pharmaceutical Engineering*, *28*(3), 24.
[23] Holm, P., Allesø, M., Bryder, M. C., & Holm, R. (2017). Q8 (R2) Pharmaceutical Development. ICH quality guidelines: an implementation guide, 535-577.

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2. Impact #@IMP-ACT-IA@#

2.1. Project's pathways towards impact

All below mentioned Impacts and Expected Outcomes, stemming from the call text (HORIZON-HLTH-2023-DISEASE-07) and addressed by ERDERA are aligned with three Sustainable Development Goals and their respective chosen targets:

- SDG3:
  - By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being.
- SDG9:
  - Enhance scientific research, upgrade the technological capabilities of industrial sectors in all countries, in particular developing countries, including, by 2030, encouraging innovation and substantially increasing the number of research and development workers per 1 million people and public and private research and development spending.
- SDG 10: Reduce inequalities:
  - Target 10.2: By 2030, empower and promote the social, economic and political inclusion of all, irrespective of age, sex, disability, race, ethnicity, origin, religion or economic or other status.

Each of the ERDERA's target has been labelled accordingly to identify specific actions that will contribute to the respective SDGs and their targets.

Expected Outcome (EO)1	***2.1.1 The EU is reinforced as an internationally recognised driver of research and innovation in rare diseases (RD) and thereby substantially contributing to the achievement of the Sustainable Development Goals related to rare diseases***	
	Already achieved/available	**ERDERA's target (game changers by 2034) (SC-scientific, SOC-societal) (ET-economic/technological)**
Contribution to EO (including scale & significance)	EJP RD funding programme allowing on annual alignment of involved funders (33 funders). Call for EU Rare Diseases Action Plan published as part of Rare2030 strategy. Dedicated widening measures have been put in place to accelerate participation of underrepresented countries + EJP RD proof-of-concept for National Mirror Groups organisation + Expansion of ERNs to new sites (often from underrepresented countries) translating to new patient populations, researchers, academic and clinical partners availability to Partnership. Biological pathways building methods (WikiPathways), Treatabolome, PCOMs/PROMs repository ATMPs platform models (e.g. Bespoke Gene Therapy Consortium) coupled to EU (distributed) excellence in the field.	**(SOC, SDG3, 10) Joint EU RD research strategy framework** designed to optimise limited resources through decisive investment addressing unmet needs of underrepresented RDs and therapy development gaps for all conditions (38 funders, industry associations, European Commission, charities) **(SC, SDG10) The asymmetry of knowledge and skills is closed, and national leverage potential** (including underrepresented countries) **is maximised** & tailored solutions provided (funding, education, expertise). Specific needs and expectations of UCs addressed, collaboration fostered, and inclusion of UCs - researchers and patient populations - in R&I programmes boosted. **(ET, SC, SDG3, 9)** ERDERA focus on implementation including: (ii) **enhanced,** generically applicable and scalable **diagnostic** solutions, (iii) generalizable models for **use of primary healthcare, population-based and cohort study data (15** models**), (iv) a blueprint and inventory for regulatory-grade RWD data sets, and (v) innovative drug development tools** (2), **(i) ATMPs technology accelerator** generating tech disruption, accompanied by standardization and regulatory compliance/acceptance available to the community. **(ET, SDG9) ATMP** technology and clinical support and expertise in one place accelerating implementation of related **clinical studies** and increasing the **attractiveness of the EU ecosystem for companies**.

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	Diagnostic research framework that is based on a few ERNs and enables research re-analysis of undiagnosed RD patients (Solve-RD)	**(SOC, SC, SDG3, 10)** Diagnostic research solution that fosters equal opportunities for (participating) EU countries to deliver timely diagnostics to patients with rare diseases, and (ii) establishes the foundation of an internationally coordinated and federated diagnostic research program for suspected RD patients which could not be diagnosed in the diagnostic setting.
Target groups	PLWRD, industry/private sector, research community, regulatory authorities, public decision makers, healthcare providers & authorities	
Requirements & potential barriers	Fast-paced changing technologies impacting both the research strategy framework and new technological developments. New pharmaceutical Directive and Regulation impact the development of new RD therapies (including ATMPs)	
Mitigation measures	Governance & management structure of ERDERA is equipped with robust horizon scanning to detect technological progress and any forthcoming legislation/regulatory changes on time and encompass it within strategic R&I agenda and investments. Establishing a Dedicated Task Force for Regulatory Adaptation and Technological Innovation & Enhancing Collaboration with Regulatory Bodies (WP18) Strengthening Partnerships with Technology and Pharmaceutical Companies (WP21) Enhancing Collaboration with Regulatory Bodies (WP20) Implementing Advanced Data Analytics and AI for Horizon Scanning (WP1 & WP15) Creating a Flexible Funding Mechanism (WP3) Use PPIE activities to provide valuable insights into the practical impacts of technological and regulatory changes. Promoting International Collaboration and Knowledge Exchange to expand international collaboration with other countries and regions (WP25)	
Expected Outcome (EO)2	***2.1.2 Research funders align, adopt and implement their RD research policies allowing for the optimal generation and translation of knowledge into meaningful health products and interventions responding to the needs of people living with a rare disease across Europe and globally***	
	Already achieved/available	**ERDERA's target (game changers by 2034)**
Contribution to EO (including scale & significance)	A pre-existing joint support for multinational research projects through competitive funding often considered as the only source of RD-specific funding at national level (83.5 M€ invested in EJP RD). Research component in RD strategies/plans in only few countries. EU infrastructures to support pre & clinical research (e.g. EATRIS, ECRIN, BBMRI, INFRAFRONTIER, C4C) + Proof-of-concept for RD expertise support services of EJP RD including reusable data generation (FAIRification). RD Patients represented in the governance of different RD programmes + EJP RD concept for patients funding in research projects.	**(SOC, SC, SDG3, 9)** Long-term commitment and **sustainable multination funding** to support of basic, translational and clinical research (commitment to ERDERA of 167.5 M€ in cash without associated partners, and up to 180.8 M€ in cash with the inclusion of associated partners), and **integrated in national RD strategies/plans (for at least 50% of involved countries).** **(SC, SDG9) Integrative expertise support and shepherding** timely accessible and deployed at all levels of project development (for at least all projects to be funded within the Partnership & offered as sustainable service after the lifetime of the Partnership grant) + data services ecosystem to ensure reusability of ERDERA funded research projects results. **(SOC, SDG10) PLWRD are equal partners** in **all stages** of the research process including governance and execution. **All ERDERA funded projects** include PLWRD as co-designers (minimum of 100 projects).
Target groups	Funders, policy makers, research community, PLWRD, research infrastructures, healthcare providers & authorities	
Requirements & potential barriers	Overarching socio-political forces driving national prioritization/roadmaps and impacting long-term commitment to RD funding and research infrastructures.	
Mitigation measures	ERDERA's communication & dissemination strategy to policy makers to highlight the importance of RD research and the need for sustained funding (including for example, Utilizing real-life stories and data on the impact of RDs to foster a supportive socio-political environment). Implementation of National Mirror Groups to drive alignment of priorities between national stakeholders and ERDERA. Expand funding Mechanism to other source of funding (public-private collaborations, international collaboration and funding agreements Strategic Use of Data and Evidence: Generate and disseminate compelling evidence on the socio-economic benefits of investing in RD research, including potential savings for healthcare systems and improvements in patient outcomes (WP10)	

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Expected Outcome (EO)3	***2.1.3 The RD research community at large benefits from and use an improved comprehensive knowledge framework integrating the EU, national/regional data and information infrastructures to improve translational research***	
	Already achieved/available	**ERDERA's target (game changers by 2034)**
Contribution to EO (including scale & significance)	**RD Ontology** (ORDO) and **RD knowledge bases** (Orphadata, Treatabolome, RD-WikiPathways) and **repositories** (RD PCOMs/PROMs), implementable data standards, FAIR standards and methods, EJP RD Virtual Platform model, tools and specifications + ERN registries and other RD-Ready resources like ERDRI, 1+Million Genomes/GDI, national initiatives to create data hubs and EHDS. **Data Analysis Task Force/Data Interpretation Task Forces** collaborative model for solving the unsolved RD (Solve-RD) **Close collaboration with initiatives** such as the Critical Path Institute (C-PATH), the Global Alliance for Genomics and Health (GA4GH), the Research Data Alliance (RDA), EOSC, EHDS, bridging public, private and regulatory bodies joint undertakings.	**(SC, ET, SDG3, 9)** ERDERA's **Data Service Hub** (as CRN and funded projects core support structure) orchestrating the FAIRification of existing and newly collected research and clinical data (including from funded research projects & CRN), linking Health & research data from EU, international to National level and enabling its exploitation to generate high-quality, regulatory compliant evidence to guide diagnosis and development of treatments. **(SC, ET, SDG3)** Data Analysis Task Force/Data Interpretation Task Forces collaborative model brought to the next level so that newest-technologies-based discoveries and the federated diagnostic research approach enable an agile and continuously growing diagnostic research knowledge base.
Target groups	Research community, patient organisations, research infrastructures, regulators	
Requirements & potential barriers	Fast moving technologies impacting uptake of proposed solutions. National and EU data-related regulations and legislations. Possible lack of manpower at certain levels (especially healthcare provider/hospitals) and lack of mutual trust and understanding amongst the stakeholders impacting research-healthcare interactions.	
Mitigation measures	Governance & management structure of ERDERA is equipped with robust horizon scanning to detect technological progress and any forthcoming legislation/regulatory changes on time and encompass it within strategic R&I agenda and investments. Continuous dialogue with regulators (EMA, FDA) and national authorities as part of the strategic and research activities to ensure two-way feedback and backed by ethical, legal and IPR expertise on data access and reuse of ERDERA. Establishment of CRN that encompasses both research and clinics components. Funding provided for data management within ERDERA funding schemes and CRN. Communication dedicated to different types of stakeholders fostering information on data sharing, its ELSI aspects, challenges and benefits.	
Expected Outcome (EO)4	***2.1.4 People living with a rare disease benefit from a more timely, equitable access to innovative, sustainable and high-quality healthcare, taking stock of highly integrated research and healthcare systems***	
	Already achieved/available	**ERDERA's target (game changers by 2034)**
Contribution to EO (including scale & significance)	European Reference Networks as backbone of clinical/research expertise. Innovation in space of CT methodologies (EJP RD, Asterix, Ideal, Inspire) & RD PROMs (ERICA). First large diagnostic research re-analysis performed by Solve-RD provided cost-effective model for collaborative diagnostic research leading to additional >10% diagnosis of included undiagnosed RD patients.	**(SOC, SC, ET, SDG3, SDG9)** Sustainable European Clinical Research Network bridging ERNs expertise and capacity with technological infrastructure (Data Service Hub) as well as methodology and regulatory support (Expertise Hub) to generate high-quality evidence for diagnosis and treatment development acceleration. **(SOC, SC, ET, SDG3, 10) Scalable and federated diagnostic pipelines, workflows and solutions** empowering national diagnostic centres and stakeholders, encompassing EU & Associated countries and based on shared standards, guidelines, knowledge bases and practices allowing on acceleration of diagnosis and solving of at least 20% of unsolved cases. Translation/operationalisation of research outputs in clinical settings is accelerated by National Mirror Groups.
Target groups	PLWRD, healthcare providers, researchers, research infrastructures, general public, EU and national policy makers	
Requirements & potential barriers	Political support to European Reference Networks and their integration in national healthcare systems. Member States readiness level (technological and legal – related to (re)use of healthcare data) to integrate proposed healthcare/diagnostic solutions.	
Mitigation measures	Focus on demonstration of clear outputs and impact via Partnership's maximized dialog with key stakeholders (policy makers, hospital managers) as part of communication & dissemination actions as well as regular key point on the agendas of National Mirror Groups and Governing Board.	
Expected Outcome (EO)5	***2.1.5 Researchers, innovators - as well as people living with a rare disease and their advocates (as co-creators) - effectively constitute and operate into an integrated research and innovation ecosystem to deliver cost-effective diagnosis and treatments***	

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	Already achieved/available	ERDERA's target (game changers by 2034)
Contribution to EO (including scale & significance)	EJP RD programme encompassing about 85% of European RD research community (mostly consisting of public sector researchers from different academic and medical disciplines, research infrastructures as well as RD patients and representatives). Diverse and dispersed training offer covering different types of stakeholders and topics often comprised at national/regional level.	**(SC, SOC, ET, SDG3, 10)** Consolidated **Alliance, geographically comprehensive and encompassing all types of actors** along the health and research value chain (171 partners in ERDERA). Targeted expansion to Eastern Europe and North Africa, through the approach to underrepresented countries from these geographical areas. **(SC, SDG10) Training** delivered **as integrative part of the research pipeline** (at least 180 trainings delivered, 10000 stakeholders trained, 8M€ dedicated): (i) to educate new generations of RD clinicians/researchers, (ii) to upscale expertise of stakeholders, (iii) to empower patients as equal partners in research.
Target groups	Researchers, research infrastructures, PLWRD, industry, funders	
Requirements & potential barriers	Member States ability to maximise and/or integrate the EU-level ecosystem created by ERDERA at national level and to feed in the Partnership with limited resources.	
Mitigation measures	National Mirror Groups supported by ERDERA as key players in national-EU alignment. Specific activities targeted specially to underrepresented countries to build/increase their capacities. Targeting of additional sources of funding like structural funds.	
Expected Outcome (EO)6	***2.1.6 Public and private actors, including civil society (e.g. NGOs, charities), establish coordinated and efficient multi-stakeholder collaborations at EU and national (including regional) levels, allowing for more effective clinical research, for example aiming at improved success rates of therapeutic development***	
	Already achieved/available	**ERDERA's target (game changers by 2034)**
Contribution to EO (including scale & significance)	Growing interest from industry & eagerness to create new funding/collaborative models (e.g. initiatives like Together4RareDiseases, RD Moonshot). Call from PLWRD on integration of all stakeholders to boost RD research (Rare 2030 recommendations). Other public-private partnerships/initiatives (e.g. IHI, EUREKA)	**(SC, SOC, ET, SDG9)** Consolidated **Alliance breaking the silos between sectors** (public 141/ private 30 [including but not limited to 12 organisations from the pharmaceutical industry sector, 7 SMEs, 5 non-for profit organisations]) **and communities** (researchers, patients PAOs, healthcare providers, regulators) and **building bridges to new groups** of countries in Europe and beyond (at least 20 new stakeholders/institutions involved). **(SC, ET, SDG9) Public** early-stage investment (167 M€ committed by beneficiaries, [180.8M€ committed by beneficiaries and associated partners]) **coordinated with** later stage investment by **private sector and philanthropy** (7.3 M€ current contribution to ERDERA maintained or increased).
Target groups	Researchers, industry, research infrastructures, funders, PLWRD, healthcare providers, regulators, policy makers	
Requirements & potential barriers	Reliance on other sector(s) continued interest (e.g., private sector) and heterogeneity of regional readiness to engage on long-term.	
Mitigation measures	ERDERA's activities as demonstrators for mutual value creation (e.g., integration of innovative research, technology and clinical activities under one umbrella). Governance adapted to encompass and focus on joint priorities.	

2.1.7 In addition, ERDERA will contribute to the following overarching impacts of the Work Programme destinations in Horizon Europe:

Impact	*Health **burden of diseases in the EU and worldwide is reduced** through effective disease management, including **through the development and integration of innovative early diagnostic and therapeutic approaches**, personalised medicine approaches, **digital and other people-centred solutions for health care**. In particular, **patients are diagnosed early and accurately** and **receive effective, cost-efficient** and affordable **treatment**, including patients with a rare disease, due to **effective translation of research results into new diagnostic tools and therapies***
ERDERA's contribution **(SDG3, 9)**	Developed scalable and federated diagnostic pipelines, workflows and solutions, using reference data (ontologies and knowledge bases) and healthcare data (EHRs), improving pre-natal and post-natal RD diagnostic rates and generating shared standards, guidelines, practices and knowledge basis will empower national diagnostic networks, centres and stakeholders allowing a significant acceleration of diagnosis and solving of at least additionally 20% of undiagnosed cases compared to state of the play in 2023. The development of treatments will be accelerated, and costs potentially reduced by providing standardized and regulatory compliant technological platform solutions for ATMPs and N-of-few therapies. The effective translation for research into tangible results will be accelerated through their design with patients, mentoring

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	and careful implementation of all funded projects (estimated min. of 80-100 of projects). Personal and societal RD burden will be decreased by the provision of tools for better functional evaluation of patients and by facilitating the development of patient-centred research and personalized approaches.
Impact	***Health care systems benefit from strengthened research and innovation expertise, human capacities and know-how*** *for combatting communicable and non-communicable diseases,* ***including through international cooperation****. In particular, they are better prepared to respond rapidly and effectively to health emergencies and are able to prevent and manage communicable diseases transmissions epidemics, including within healthcare settings.*
ERDERA's contribution **(SDG10)**	EU Clinical Research Network ERDERA's structure based on the combination and interweaving of research, clinical, methodological, data, regulatory and technological expertise and training backed by the involvement of PLWRD at all levels will directly feed into a strengthen healthcare ecosystem. All aspects of ERDERA encompass international dimension and thus ensure mutual knowledge sharing and timely access to additional resources.
Impact	***Patients and citizens are knowledgeable*** *of disease threats,* ***involved and empowered to make and shape decisions for their health****, and better adhere to knowledge-based disease management strategies and policies (especially for controlling outbreaks and emergencies).*
ERDERA's contribution **(SDG10)**	PLWRD involved at all levels of ERDERA (governance, strategy, research, etc.) are empowered by tailored processes, support, and training. Communication activities targeted to PLWRD but also other stakeholders including general public increase the knowledge on RDs.

European Partnership [European Rare Diseases Research Alliance]		**2.1.8 Monitoring and evaluation framework, version 1, [18/09/2023]**		
Overall vision: to improve the health and well-being of 30 million persons living with a rare disease in Europe, **by making Europe a world leader in RD research and innovation**, and delivering concrete health benefits to rare disease patients, through better prevention, diagnosis and treatment.				
	What is a measure of success?	**Which is the data source | and methodology used** [project data, study, ….] **| Unit of measurement**	**Who is responsible for monitoring and providing the data/ information When will it be collected?**	**Baseline and target**
GO1	Rate of diagnosed rare diseases cases	CRN & national RD diagnostic centres (Standard annotations (e.g., through 'semantic tags' for diagnosed and undiagnosed) | The increase of acceleration of undiagnosed cases | (measured percentage)	**Responsible:** CRN diagnostic research leaders (WP6-8) & Monitoring task leaders in coordination with national RD diagnostic centres. **Assessment frequency:** Y3 & Y7.	**Baseline:** 10-12,5% increase in (genomic) diagnostic rate**. Target: Y3:** 15%. **Y7:** 20%
GO1	Time to diagnose patients with a rare disease.	ERN registries | Improvement in the time to diagnoses of patient seeking medical attention for an unknown condition/ qualitative	**Responsible:** Data Services Hub, Monitoring task leaders. **Assessment frequency:** Y7/Y10.	**Baseline:** 4 years. **Target: Y7:** Time to diagnose decreases . **Y10:** Time to diagnose decreases
GO2	New therapies approved for rare diseases	ERDERA publications, surveys; clinicaltrial.gov, EudraCT, FDA & UK(MHRA) reports and Databases, Orphanet | Number of new therapies where ERDERA resources (Human expertise, developed tools, etc.) are/have been involved, as reported by the ERDERA partners and connected initiatives | Number (new therapies approved for rare diseases)	**Responsible:** ERDERA monitoring task leaders & reporting system. **Assessment frequency:** >7Y (Y10).	**Baseline**: number of existing RD therapies (as in Orphanet 2023). **Target: Y10:** at least 5% of new therapies approved by EMA developed with the support of ERDERA
GO2	Clinical Trial Readiness	Same as above GO2 indicator | Number of Clinical Trial Applications (CTAs) where ERDERA resources (Human expertise, developed tools, etc.) are/have been involved, as reported by the ERDERA partners and connected initiatives | Number of approved CTAs	**Responsible:** Task leaders (CRN and RD funding workstreams) and contact-person of the connected initiative (listed in the SRIA annex1). **Assessment frequency:** Y3 and Y7.	**Baseline:** 0. **Target: Y3:** 5. **Y7:** 10
GO3	Policy changes related to RD burden	NMGs Annual investigations (national plans/ surveys, Reports) | Policy changes refer to modifications made to existing rules, guidelines, or procedures by governments or organizations aiming	**Responsible:** To be collected annually by the National Mirror Groups. **Assessment frequency:** Y3 and Y7.	**Baseline:** 0. **Target: Y3:** TDB. **Y7:** TBD.

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		to improve the assessment and understanding of the impact and challenges posed by Rare Diseases on individuals and society. Initiatives are specific actions contributing ultimately to policy changes. The measurement of these will consider only those impacted by ERDERA activities | Number of policy changes or initiatives at local, national, and international levels aimed at addressing the impact of rare diseases on patients, families, and society.		
GO3	Funding for research on the impact of rare diseases in patients, families, and society	ERDERA Funding workstream and In-house research financial & administrative data (managed by the ERDERA call application portal that is part of the monitoring system) | ERDERA funding dedicated to research activities on the impact of RD on patients, families and society | Million €	**Responsible:** ERDERA monitoring task leaders & reporting system in coordination with the RD Funding workstream and In-house research . **Assessment frequency:** Y4 and Y7/Y10.	**Baseline:** Historic data from EJP RD (11.5M€). **Target: Y4:** TDB. **Y7:** increased by 50%. **Y10:** TBD
SO1	Projects outputs translated into innovative RD (research) models/solutions	ERDERA Monitoring and reporting system/ Total number of RD research projects supported by the Partnership (or a previous co-fund on Rare Diseases) resulting in new Clinical Studies, guidelines and patent applications/ Number	**Responsible:** ERDERA monitoring task leaders. **Assessment frequency:** Yearly from year 3.	**Baseline:** 0. **Target: Y3:** 10. **Y4:** 15. **Y5:** 20. **Y6:** 25. **Y7:** 30.
SO1	Public-private collaborations	Coordination and Management workflow & monitoring and reporting system | Collaborations between academia and for profit and/or non-profit organisations to develop and implement medical and holistic interventions for RD (MoUs/ Letters of intents/Agreements/Pilots) | Number of new collaborations	Responsible: ERDERA Coordination team. Assessment frequency: Y3, Y5 and Y7.	**Baseline:** Historic data from EJP RD (4 collaborations). **Target:** Y3: 5. **Y5:** 10. **Y7:** 18.
SO2	Access to data sources	ERDERA Data Hub & monitoring | Number of healthcare and research data sources that are onboarded and made available for scientific and regulatory evaluation and healthcare delivery | Number	**Responsible:** Data services Hub. **Assessment frequency:** Every 2 years.	**Baseline:** 20 (resources already onboarded on the EJP RD Virtual Platform). Target: **Y2:** 25. **Y4:** 30. **Y6:** 40.
SO2	Use of data sources	ERDERA Data Hub & monitoring system | increase of access to research data sources through the Virtual Platform | %	Responsible: Data services Hub Work Packages leaders. Assessment frequency: Yearly.	**Baseline:** Number of VP Access at the end of EJP RD. **Target: Y0:** +5% **Y1:** +5%. **Y2-Y5:** +10% every year . **Y6-Y7:** +5% every year
SO3	Capacity building of RD patients	Training activity surveys & monitoring system | Number of patients empowered, within the Partnership, through capacity-building and training activities related to research | Number patients participated at training activities per year	**Responsible:** Workstream Education and Training leaders & PPIE. **Assessment frequency:** Yearly.	**Baseline:** Historic data from EJP RD : 350 per year. **Target:** Y1-Y7: 2500-3000 every year
SO3	Patients involved in RD funded projects	Funding workstream reports; Project reports; & monitoring system | Percentage of funded research projects that involve patient organisations as co-designers. | Percentage	**Responsible:** RD funding Workstreams leaders & PPIE. **Assessment frequency:** Yearly.	Baseline: Historic data from EJP RD: 60%. **Target: Y1:** 70%. **Y2:** 75. **Y3:** 80%. **Y4:** 85%. **Y5:** 90%. **Y6:** 95%. **Y7:** 100%
SO4	Transdisciplinary training programmes as part of the RD research educational pipeline	Data & Reports from Workstreams Education and Training & Inter(National) Capacity Alignment workstream & monitoring system | Number of transdisciplinary research training programs developed and implemented at the European level | Number	**Responsible:** Workstream Education and Training leaders. **Assessment frequency:** Year 3, 5 and 7.	**Baseline:** 15 transdisciplinary programmes in EJP RD. **Target: Y3:** 60. **Y5:** 120. **Y7:** 180

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SO4	Alignment of capacity and skills at national / local level	Data & Reports from Workstreams Education and Training & Inter(National) Capacity Alignment workstream & monitoring system | Number of national/local training and education programs aligned with ERDERA (at least 1 training per Country; 37 Countries) | Percentage	Responsible: Education and Training & Inter(National) Capacity Alignment leaders. Assessment frequency: Y3, 5 and 7.	**Baseline:** 0. **Target: Y3:** 4%. **Y5:** 50%. **Y7:** 100%
SO5	National RD research and Innovation Integration	Coordination and Management workflow & monitoring system / Number of countries with national RD research strategies aligned with EU and international collaborations supported by the Partnership | Percentage	**Responsible:** Coordination team & International Alignment Workstream leaders & NMGs. **Assessment frequency:** Y3, 5 and 7.	**Baseline:** 0. **Target: Y3:** 10. **Y5:** 30. **Y7:** 50.
SO5	ERDERA RD research and Innovation synergy with other programs	Coordination and Management workflow & monitoring system | Number of complementarities and synergies established with other relevant programmes and initiatives | Number	**Responsible:** Coordination team & International Alignment Workstream leaders. **Assessment frequency:** Y2, 4 & 6.	**Baseline:** 0. **Target: Y2:** 2. **Y4:** 5. **Y6:** 7.
OO1	Progress towards (financial and in-kind) contributions from partners other than the Union	Funding workstream reports & monitoring system | Percentage of contributions achieved out of total commitments made by the ERDERA partners other than the European Commission at the beginning of the partnership/ Million € i.e., committed vs. actual	**Responsible:** Funding workstream WP and task leaders & coordination team. **Assessment frequency:** yearly .	**Baseline:** 167M€ of in cash and 37M€ of in kind commitment. Target: **Y10:** At least initial commitment achieved
OO1	JTC funding spending for research	Funding workstream reports & monitoring system | Amount of funding provided to researchers through JTCs | Million €	**Responsible:** Funding workstream WP and task leaders. **Assessment frequency:** yearly.	**Baseline:** 26,5 M€ committed for the 1st year of ERDERA. **Target: Y7 :** 76,8 M€
OO2	Integrated Data Service's infrastructure	ERDERA Data-Hub, monitoring system & coordination and Management workflow / Services provided by the integrated data infrastructure/ Number	**Responsible:** Data Service Hubs WP and task leaders, and Coordination team. Assessment frequency: yearly.	**Baseline:** 0. **Target: Y1:** 30. **Y2:** 50. **Y3:** 70. **Y4:** 90**. Y5:** 110. **Y6:** 130. **Y7:** 150.
OO2	Integrated Expertise Service's infrastructure	ERDERA Data-Hub, monitoring system & coordination and Management workflow | Services provided (i.e., ELSI, IPR, regulatory, methodology, etc.) by the integrated expertise infrastructure | Number	**Responsible:** Expertise & Data Service Hubs WP & Task leaders, and Coordination team. Assessment frequency: yearly.	**Baseline:** 0. **Target: Y1:** 20. **Y2:** 25**. Y3:** 30. **Y4:** 35. **Y5:** 40. **Y6:** 45. **Y7:** 50.
OO3	NMGs created/ functioning	International Capacity Alignment workstream (WPs) reports & ERDERA monitoring system | Total number of NMG operational | Number	**Responsible:** International Capacity Alignment WP and Task Leaders. **Assessment frequency:** Y1 and Y2.	**Baseline:** 4. **Target: Y1:** 14**. Y2:** 31.
OO3	Interactions/projects with non-EU entities	International Capacity Alignment workstream (WPs) reports & ERDERA monitoring system | Total number of interactions (e.g., good practices, harmonisation)/projects with International legal entities | Number	**Responsible:** International Capacity Alignment WP and Task Leaders. **Assessment frequency:** yearly.	**Baseline:** 0. **Target: Y1:** 1. **Y2:** 2. **Y3:** 3. **Y4:** 4. **Y5:** 5. **Y6:** 6. **Y7:** 7.
OO4	Capacity building	Data & Reports from Workstreams Education and Training & ERDERA monitoring system | Number of researchers/stakeholders having benefited from upskilling activities (through training, mobility, and access to infrastructures) | Number	**Responsible:** ERDERA monitoring task leaders in coordination with training leaders & contributors. **Assessment frequency:** yearly.	**Baseline:** Historic data from EJP RD : 2500-3000 per year. **Target: Y1:** 4640. **Y2:** 6285. **Y3:** 8150. **Y4:** 8760. **Y5:** 9360. **Y6:** 9960. **Y7:** 10570.
OO4	Funding invested into capacity building activities	ERDERA monitoring system & coordination and Management workflow, ERDERA periodic reports | Total Funding committed for training, mobility, and access to infrastructures | Million €	Responsible: ERDERA Coordination team & ERDERA monitoring task leaders. Assessment frequency: yearly.	**Baseline:** Historic data from EJP RD : 6.5M€ (overall budget for Training & education activities). **Target:** Y1-Y7: commitment every year of 1.2M.

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OO5	Expansion to new stakeholders	ERDERA monitoring system & coordination and Management workflow | Number of new stakeholder (by category) involved with ERDERA after launch | Number by category of stakeholders	**Responsible:** ERDERA Coordination team & ERDERA monitoring task leaders. **Assessment frequency:** yearly	**Baseline:** 94 beneficiaries in EJP RD, and 152 beneficiaries + 19 associated partners in ERDERA. **Target: Y1:** +10. **Y2:** +5. **Y3:** +3. **Y4-7:** +1 every year.

2.2. Measures to maximise impact - Dissemination, exploitation, and communication #@COM-DIS-VIS-CDV@#

ERDERA builds on EJP RD's legacy to continue making a difference in RD research in Europe and beyond. Extensive (inter)national multi-stakeholder collaboration in communications and dissemination activities enabled by this large partnership will be key to advance ERDERA objectives and ensure effective engagement with key audiences who will either: (i) **use and/or benefit** from ERDERA activities and research outcomes (mainly patient and RD research communities at large); (ii) **contribute to develop** solutions for RD research (mainly funders; industry; healthcare providers; research infrastructures or other RD research initiatives); (iii) **intervene in shaping** the RD ecosystem (mainly public decision makers at national and international level; regulators; other RD consortia; Media or society at large). The Communication (C) and Dissemination (D) strategy will be developed and implemented by WP2, in concurrence with all work streams, with a view to paving the way for future sustainability and successful exit strategy (WP1). It will strive to: (1) **Raise awareness about ERDERA** with a focus on describing the important progress made to date, identify existing gaps in RD research and outline plans to address current and future challenges. (2) **Generate interest on ERDERA strategic and operational goals**, expected outcomes and long-term impacts and continue building a global community of interest around RD research. (3) **Maximise promotion of funding calls and available RD research assets and services** (data services; accelerator hub; CRNs, training, mentoring), especially amongst underrepresented countries and/or underserved groups. Facilitate that outputs are not only published and widely disseminated but ultimately adopted by the RD research community, starting with applicants and funded projects. (4) **Inform about progress and results achieved by ERDERA funded initiatives** reinforcing the reputation of this European partnership as an enabler of far-reaching, trans-national RD research. (5) **Amplify patients' voice** throughout ERDERA communications and actively engage with the general public through awareness campaigns. (6) **Support engagement, networking and (inter)national capacity alignment** activities to enable debate, mutual-understanding, alliance building and knowledge exchange across the global RD ecosystem.

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The diverse expertise and long-term experience in the field of RD research brought together by ERDERA will facilitate adequate understanding and access to the following key audiences:

RESEARCHERS as architects and leaders of ERDERA investigational projects, as well as users of its resources and services and future adopters of results and standards generated within the Partnership. This audience includes academia, clinical and industry researchers (Systems Biologists; Data scientists; Biobank managers; Laboratory scientists & technicians; Clinical geneticists) and focuses on ERDERA funded research, Research organisations, Learned societies, Professional associations (i.e., CGCOM; CENOM), applicants to ERDERA funding calls or academic institutions and universities (medical & biomedical students, lecturers, university managers; organizations of academic institutions (i.e., UEMS)).

PATIENTS, actively involved in the design of RD research as key drivers and ultimate beneficiaries. This broad audience group comprises patients- organisations and patients and care givers and, specifically ePAGs (RD patient representatives involved in ERNs) and YPAGs (Young Patient Advisory Groups).

FUNDERS as scouters and supporters of promising RD research projects ranging from philanthropic organisations, (inter)national public funding bodies or venture capital.

INDUSTRY/PRIVATE SECTOR as developers, investors and adopters of RD solutions. This audience involves researchers and innovation managers specialising in drug development, medical devices, ATMPs, ICTs at large pharmaceutical companies, SMEs and Biotech. Associations such as EFPIA and EUCOPE are key interlocutors.

RESEARCH INFRASTRUCTURES as experts in translating promising ERDERA funded research into real solutions for patients. Represented by organisations such as ESFRI.

HEALTH CARE PROVIDERS as testers and potential adopters of solutions developed in the context of ERDRA, especially those organised around the **ERNs** but also international organisations (EUHA), Hospitals and Clinicians at large.

2.2.1 Communication and dissemination strategy

The overarching communication and dissemination strategy will be designed by WP2 (Task 2.1) by Month 6. It will build on EJPRD past experience and achievements and ensure alignment across the different work streams so that all activities reflect consistently ERDERAs vision, objectives, roadmap and expected impacts. The strategy will be implemented through Annual Work Plans developed in concurrence with work stream leaders. Given the broadness and multi-disciplinarity nature of ERDERA, a communications officer will coordinate and support T2.2. Likewise, a science writer will be appointed to facilitate understanding of ERDERA's ambition, progress, services, results and their potential impact across a diversity of audiences. Editorial content curation will observe **science communication best practices** (i.e., avoid jargon, provide examples, summarise ideas, contextualise, start with key findings, etc).

Task 2.1. will follow a tested methodology to design a sound communication and dissemination strategy which will be driven by clear objectives. Building on EJPRD reputation and results, objectives will gradually steer from raising awareness and interest in ERDERA -vision, goals, work plan, funding calls, existing and newly created resources and results and expected impacts- towards facilitating understanding, acceptance, endorsement and, ultimately, adoption of the different solutions generated both by the partnership and the research being funded by it. Critical to develop this strategy is to ensure in-depth understanding of key audience group's needs, motivations and attitudes. To this end, WP2 will **map out each audience** with the collaboration of work streams with a view to start shaping a unique value proposition and tailor operational communication objectives and main messages accordingly. By performing this pre-emptive analysis, audiences will be properly segmented and analysed from a work stream perspective to be addressed through the most appropriate channels, tools and activities. **An outline of the envisaged communication and dissemination activities can be found in this table:**

	Main target audience	Objective	Description of tools & activities
Coordination	All	Generate awareness & interest about ERDERA objectives (SRIA), work plan, major developments and expected impacts. Set up and manage general communication tools, channels and resources.	**Branding** (logos, templates, etc). Website (general & sub-sites/platform). **Newsletters** (general & segmented). Animated videos / Video interviews. **Slide deck** (general & per work streams). **Factsheets** (general & per work streams). **Podcast series** (3 episodes per year feeding from all work streams). Infographics.

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	Public decision makers Funders, Regulators, Patient organisations, Researchers, Industry (EFPIA/ EUCOPE), Healthcare providers, Other (IRDiRC; ESFRI), Media	Support engagement with key stakeholder groups to align on RD policy research strategies, regulatory, legal and ethical issues. Raise interest and understanding around these topics.	Organisation or participation in **conferences, seminars, workshops or focus groups**. Develop **editorial content** to be shared through online channels (website) summarising public discussions, agreements, etc on current gaps in RD research, as well as EU and national recommendations or key priorities. Leverage multistakeholder. **Advisory board activities and strategy meetings**. Production and dissemination of **white papers and policy reports**. Launch **press releases**.
	Public decisions makers Public funding bodies All	Create awareness around ERDERA annual progress (T1.3). Support sustainability strategy	**Meetings with relevant authorities**. Leverage **dashboards** to produce engaging **visual summaries** to be shared through website, newsletter; social media; podcast (1 episode per year focused on progress). **Marketing of ensuing legal entity**, its value propositions and resulting services and resources. Launch **press releases**.
	Patients, Researchers, All	Strengthen patients' voice. Support production of layman materials.	Participation in **patient focused events**. Publish patient **testimonials and case studies** showcasing good patient engagement practices in RD research. **Layman resources** developed in **diverse** formats (articles, video interviews or infographics), made available and promoted online.
Funding	Researchers (Academia-Universities; Clinical - Research organisations), Patients' organisations, Healthcare providers/ ERNs, Industry, EC & other RD initiatives	Promote funding calls, webinars for candidates & public consultations. Inform of calls' results.	**Coordinated campaign** launched via ERDERA, EC & partnering organisations' online channels & promoted through external events. Contact with key people from different institutions who can relate information. **Flash newsletters. Press announcements**. **Website news** articles
	All	Publicise progress, achievements and impact of research funded by WPs 3-5. Enhance dissemination of scientific outputs.	Leverage T1.3.1.4 as a source of case studies to be featured on online channels & external events. Amplify launch of scientific publications on social media & website. Launch media pitch around newsworthy achievements.
CRNs	CRNs, Learned societies Professional, associations Researchers	Support outreach and dissemination to facilitate understanding, acceptance and adoption of data systems and tools (WP6) and newly generated evidence (WPs 7-12)	Publicise **peer-reviewed** publications, reports, case studies**, blueprints** and other resources and tools to target audiences through website articles, infographics or animated videos. Presentation at **events**.
Data Services	Joint Transnational Calls & Clinical trials applicants, CRNs / ERNs, EFPIA/ EUCOPE, Healthcare providers, ESFRI, Researchers, Patients	Increase awareness about data readiness, sharing and analysis services and new resources onboarded to the platform. Disseminate new knowledge generated on genetic cause of diseases, etc to aid adoption of methods that increases the usability of rare disease data.	**Publicise virtual platform** and signpost **accessible services and resources** in a visual format (infographic), available through main website. Articles to be **published on website** and segmented **newsletter** and shared on **social media**. New knowledge to be presented at key events (WODC, ESHG, ECRD).
Expertise Hub	Joint Transnational Calls (JTC) & Clinical trials (CT) applicants CRNs Researchers Patients' representatives	Increase awareness about mentoring, consultancy, and methodological support services.	Promote webinars and workshops and signpost guidance recommendations and tools (Innovation Management Tool) to targeted audiences via website or segmented newsletters, as well as presentations at external events.
		Dissemination of the Innovation Management Toolbox. Dissemination of the services provided by the Regulatory Support Group. Promotion of the Consultancy and Regulatory expertise database.	Publicise new features of the IMT to different stakeholders via news posts, presentations, targeted communication and dissemination.

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Training	JTC & CT applicants, EPAGs & YPAGs, ERNs, Researchers, Patients, Academic institutions, universities, Professional, organisations, NMGs	Raise awareness on existing and new training resources and educational activities	Develop an infographic describing the ERDERA training pathway, accessible through website. Promotion of existing and new training resources and activities, including courses, webinars, workshops and other events primarily, leveraging social media platforms and e-mail updates and targeting (inter) national organisations (NGOs, learned societies, universities).
Acceleration Hub	Regulators, ERNs, CRNs	Amplify dissemination of processes, methods and results produced by WP21	Promote reports, blueprints and publications through online channels (website, newsletter, social media) and off-line (presentations and webinars)
	Funders Industry Public decision makers	Increase reputation of Acceleration Hub as an enabler of translational research and promote the innovation marketplace	Produce video interviews, website articles, podcasts or animated infographics to showcase most promising/advanced projects. Launch media pitches. Promote matchmaking activities (webinars). Present acceleration hub at key events.
International Capacity	Public decision makers at large (NMGs) IRDiRC	Raise the profile of NMGs and their relevance to ensure cross-fertilisation, knowledge transfer and alignment.	Feature news stories on selected NMGs activities, achievements or good practices on website, podcast series and segmented newsletter.
		Empower NMGs to step up their communications	Facilitate access to central communication materials and resources. Provide guidance to NMGs on the design of national communication plans.
		Support IRDiRC communication strategy and highlight external alliances	Support the implementation of IRDiRC communications plan. Amplify dissemination of key activities (state of the play; annual meeting; etc) through ERDERA channels. Launch press releases.

Results and outcomes generated by the Partnership will provide policymakers and regulators with evidence-based information to aid decision-making, thus contributing to harmonise and advance rare disease research strategies at national and European level. It is expected that ERDERA will impact the establishment, revision, or revitalization of national plans/strategies for rare diseases, the diagnostics approaches at EU and national scale, the use and reuse of healthcare and research data, methodological innovation for data use and biostatistical approaches to clinical studies in small populations that are aligned/contributing to the New pharmaceutical Directive and Regulation. Critical to the successful implementation of this strategy will be the support and active involvement of all ERDERA partners in communication and dissemination activities and facilitating engagement with key stakeholders. To this end, as ambassadors of this partnership, partners are considered an intrinsic audience. Likewise, reputable leading experts involved in ERDERA will be crucial to enhance the visibility and credibility of the partnership's outcomes. Finally, the advisory bodies foreseen in ERDERA will ensure continuous multi-stakeholder dialogue and much needed debate to continue shaping rare disease research strategy and paving the way for future sustainability.

2.2.2 Sustainability and IPR management & exploitation of results

ERDERA is set to have a major impact in the rare disease research ecosystem by delivering a unique combination of services and activities. Its vision will be defined with the input from the consortium and its advisory and governing bodies and will consider elements already defined in the Sustainability Report of the EJP RD. This will guide the value proposition offered by each workstream and will evolve with the project. Data on progress of individual workstreams and results collected by the Monitoring and Strategy tasks, and by the IPR group, will be analysed to identify how and where value is created within ERDERA. This knowledge will serve to advice decision making throughout ERDERA's lifespan and inform any recommended reallocation of resources to improve success rates and maximise impact. During the first three years the consortium will foster the exit strategy and make a business case for the future legal entity. At the end of this period, a White Paper will be issued outlaying the proposal including a relevant business model and a suitable legal setting (i.e., international non-profit association) that supports the federated nature of the future *institute*. To this end, ERDERA will use learnings from existing research infrastructures (such as eBrains and EUREKA models) and will map out all services and resources across three major domains – infrastructure (Data, Expertise and Acceleration Hubs), clinical Research network and RD research funding mechanisms. In this context, it will consider administrative and legal aspects to define incentives, governance and financial (costs and revenue) frameworks of the future entity, ensuring its sustainability and growth within the RD ecosystem. The White Paper will be accompanied by an Impact Report outlaying key achievements of ERDERA and its predecessors, such as EJP RD, as well as demonstrating clear value (showcases) for public and private organisations including funding organisations and companies.

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The exploitation of results will be supported by the management of Intellectual Property (IP) which will aim to facilitate collaboration among the Beneficiaries, Affiliated Partners and Associated Partners of ERDERA (named ERDERA Partners in this section hereafter) by allowing them access to each other's Background and Results, under pre-agreed conditions and without the need for further approvals or payment of royalties. This approach, that will be described in the Consortium Agreement (CA), encourages sharing of knowledge and information among the consortium members while ensuring that the intellectual property rights of the owning ERDERA Partners are respected. For IP, the CA will address (1) the identification and ownership of Background, additional data, know-how or information; (2) the management of the Results generated including their ownership, data contributed as in-kind, transfer of ownership and granting of license, protection, commitment to exploitation, and their dissemination and communication; (3) and the Access Rights for the implementation of ERDERA, the exploitation for research use, direct exploitation, for new and departing ERDERA Partners and for Third Parties. The CA will specify the rights of ERDERA Partners to access the Background and Results of each other, both during and after the completion of ERDERA. The signature of the CA by the Beneficiaries will be considered as a valid written request and approval for Access Rights, both for research use and for the exploitation. This implies that signing the agreement grants Access Rights to the Background and Results of other ERDERA Partners as needed for the exploitation or for research use of their own Results. The Access Rights for the purpose of research use of own Results or Results of other ERDERA Partners are granted on a Royalty-Free basis. This means that the ERDERA Partners are not required to pay any fees or royalties to the owning one for accessing their Background or Results for research purposes. Access Rights are granted to the extent needed for exploitation or reasonably required for research use of own Results or Results of other ERDERA Partners. This means that the access will not be unrestricted but is limited to what is necessary or reasonable for the intended purpose. The scouting of IP aspects will be meticulously managed by a dedicated Intellectual Property Rights (IPR) support group, composed of IPR experts from different ERDERA Partners. A list of deliverables will be created for identifying and quantifying joint results, leading to an inventory of exploitable Results that will be regularly updated. The IPR support group will facilitate portfolio assessment, ensuring that exploitable Results are properly acknowledged for sustainability planning.

Summary

SPECIFIC NEEDS
High medical needs for PLWRD and significant costs for health care systems due to lack of available therapies and delayed diagnosis (30 million people in Europe living with a RD. There is no therapeutic option for 95% of RDs. The average time for diagnosing a known rare disease is > 4 years. About 50% of rare disease patients do not have a confirmed diagnosis). **Limited understanding of the real impact** RDs has on patients, carers and society. **Need to integrate into RD research and scale up the opportunities presented by most recent advances** on new ATMPs technologies and data-driven computational tools, statistical and AI methods. **Scarcity, asymmetry and fragmentation of knowledge**, skills and expertise in RD research. **Fragmentation of data ecosystem and limited interoperability** preventing research from delivering data-driven solutions. **Limited synergies in policy and strategies** in RD research within EU member states. **Lack of business model and incentives** to translate research into diagnosis and treatment solutions.
EXPECTED RESULTS
Sustainable legal entity embodying a consolidated alliance amongst all actors (public/private) intervening in the RD value chain (researchers, healthcare providers, regulators) which provides a state-of-the-art RD infrastructure for data and expertise, clinical research services, funding support and knowledge sharing. **Joint EU RD research strategy framework** & multistakeholder collaboration environment & alignment of national and local RD research activities through NMGs. **Data Service Hub** that ensures FAIRness of research and clinical data and enables this data to be exploited by linking health and research data from national, EU or 3rd country sources. Advanced **data driven** computational tools**,** statistical and AI methods. **Federated diagnostic pipeline** based on shared standards, guidelines and practices implemented in most EU countries. **Sustainable CRN** that brings together ERNs expertise and capacity with technological infrastructure, methodology and regulatory support. **Comprehensive training pathway and educational resources** widely available to researchers, clinicians and patients.
D & E & C MEASURES
Communication: General communication via website, infographics, videos, factsheets, recorded webinars, podcasts, etc. Media outreach. Social media activity. Engagement activities with stakeholder groups (webinars, meetings, workshops). Leverage case studies and testimonials as source of news stories. **Dissemination:** Publication of results in scientific journals and Open Research Europe. Policy reports, blueprints, peer reviewed publications, guidelines widely shared via ERDERA and partners' communication channels and further disseminated through participation in stakeholder meetings, conferences and other events. Dedicated promotion campaigns to increase awareness of specific results. **Exploitation:** Business case for a sustainable RD research infrastructure outlined in a white paper, accompanied by an Impact report on ERDERA achievements. Engagement with public and private organisations as users and beneficiaries or potential

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funders/investors of RD research to refine business case, accompanied by open discussion with decision makers at the EU and national level.

TARGET GROUPS

RESEARCHERS: ERDERA funded initiatives; Academia, clinical and industry researchers; Research organisations; Learned societies; Professional associations (i.e., CGCOM; CENOM); applicants to ERDERA funding calls; Universities; Academic institutions org. (UEMS)
PATIENTS: Patient organisations; PLWRD & carers; ePAGs & YPAGs
PUBLIC DECISION MAKERS: National Mirror Groups (NMGs); Ministries of Health & Research; EC; Relevant EU directorates (DG RTD, Santé, Connect); (Funding) Program directors and managers; European & National legislators focused on health & research;
OTHER CONSORTIA & ASSOC: IRDiRC; ESFRI; Other initiatives (RD Moonshot; Together4RDs)
REGULATORS & HTAs
FUNDERS: Philanthropic organisations; (Inter)national public funding bodies; Venture capital
INDUSTRY/PRIVATE SECTOR: Large pharmaceutical companies; SMEs / Biotech, medical devices, ATMPs; ICTs; EFPIA; EUCOPE
RESEARCH INFRASTRUCTURES: ESFRI & others
HEALTH CARE PROVIDERS: European Reference Networks (ERNs); (EUHA); Hospitals/Clinicians
GENERAL PUBLIC & MEDIA

OUTCOMES

- Strengthened and **integrated research and innovation ecosystem**, involving **PLWRD as co-creators**, that **delivers cost-effective diagnosis and treatments.**
- Aligned **research funding** leads to optimised generation and **translation of knowledge into health products and interventions** and fosters the approach of public early-stage investment, followed by later-stage investment from private sector and philanthropy.
- Comprehensive and standardised **knowledge framework** in place that **integrates EU, national and regional data and information infrastructure**s to improve translational research.
- Better identification pathways of consenting patients in Europe allow both **better understating of the disease and its impacts** and patients' **timely enrolment in clinical** studies and inclusion in diagnosis and research pipeline.
- Central access point to RD research supporting services **attracts high quality research projects** who benefit from cross-disciplinary expertise, tools and resources.
- Coordinated and efficient **multi-stakeholder collaboration** encompassing public and private actors at European, national and regional level.
- **New generation of clinicians, researchers and patients trained** in RD research which allows the upscale of expertise and the empowerment of PLWRD.
- **Aligned EU, (inter)national and regional research strategies** enables optimization of resources and scalability of results

IMPACTS

- EU reinforced as a **global leader** of research and innovation in rare diseases which leads to **job creation** and increases EU **competitiveness** in R&I and enhances its **attractiveness for companies**.
- In-depth understanding of RD impact on patients, families and health systems **informs research and care** and translates into **more meaningful societal support.**
- Integrated European RD research ecosystem delivers **more cost-effective diagnosis and treatments,** contributing to the **sustainability of health systems**.
- Better prevention, diagnosis and treatment of RDs brings **tangible health benefits and improved wellbeing** to > 30M patients in Europe. Long-term **contribution to** the fulfilment of **SDG** regarding RDs by delivering "1.000 new therapies for RD approved in Europe".
- **Outcome-oriented public & private investment** strategies and programmes, better contribute to **address the needs of PLWRD**.
- Integrated multi-national and multi-stakeholder R&I ecosystem for RDs contributes to **reduce inequalities across Europe** in **timely access** to innovative, sustainable and high-quality healthcare for PLWRD.
- Increased understanding on impact of RD and research across society, added to open science practices, strengthens **citizens engagement and trust in science.**

#§IMP-ACT-IA§#

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3. Quality and efficiency of the implementation #@QUA-LIT-QL@# #@WRK-PLA-WP@#

3.1. Work plan and resources

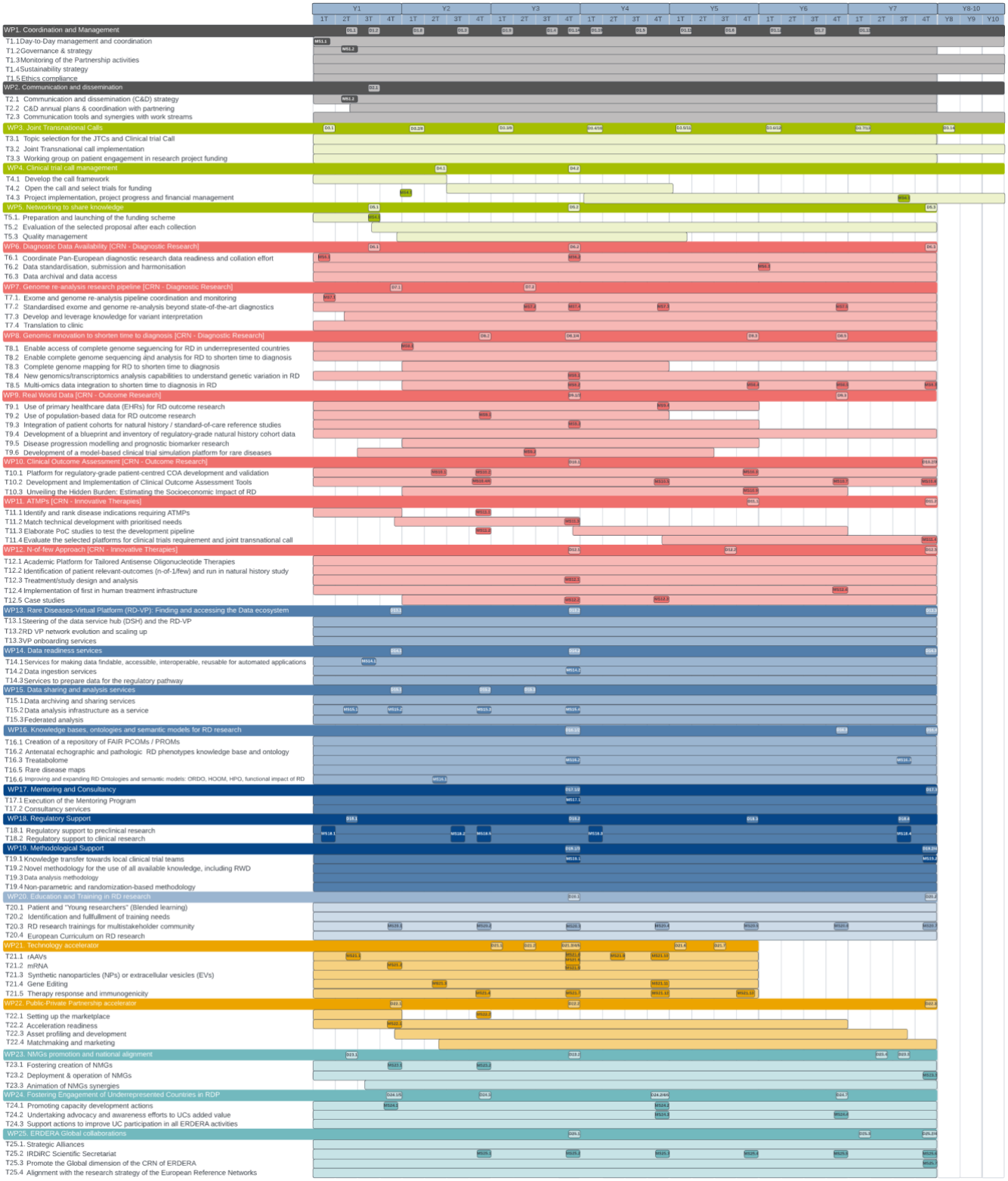


Figure 2. ERDERA Gantt chat (**zoom for details – high resolution picture**)

The overall work plan of ERDERA is organised in 3 main phases: 3+4+3 years. The first two phases - 3 years + 4 years are aligned with the provision of instalments and foreseen two Grant Agreements. The last 3 years are part of the phasing out strategy and will cover only the finalisation of funded projects and clinical trials that were granted in the last JTCs and CT call. This proposal encompasses thus the description of the overall work foreseen for 7 +3 years but specific attention is given to underline the outputs expected after the first 3 years of the project. Similarly, the detailed budgets per partner and activity described in the

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proposal encompass only the first 3 years as they correspond to the first grant instalment. The proposal, the Annual Work Plan of year 1, and the SRIA are complementary and therefore cross-referenced.

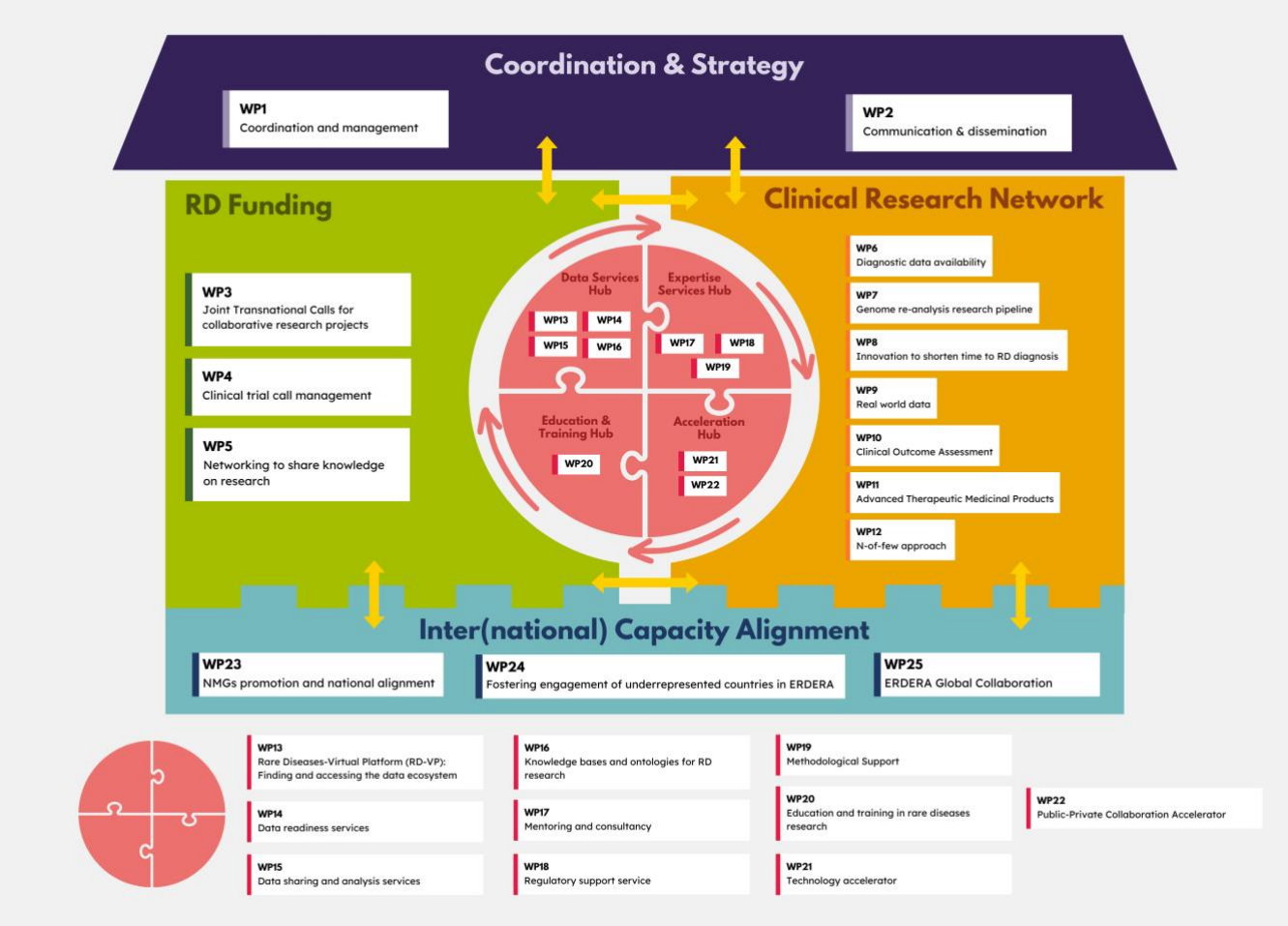


Figure 3. ERDERA PERT chart (**zoom for details – high resolution picture**)

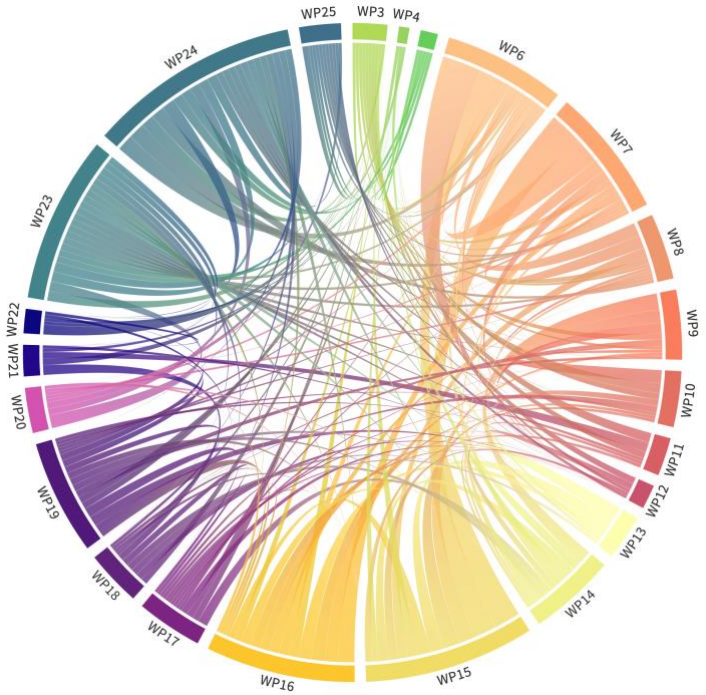


Figure 4. Directional Chord diagram displaying Work Packages Synergies and Integration based on number of cross work package milestones and activities description. Interactive chart available on: https://public.flourish.studio/visualisation/17031173/

Tables for section 3.1

Table 3.1a: List of work packages (included in Part A)

Table 3.1b: Work package description (included in Part A)

Table 3.1c: List of Deliverables (included in Part A)

Table 3.1d: List of milestones (included in Part A)

Table 3.1e: Critical risks for implementation #@RSK-MGT-RM@# **(included in Part A)**
#§RSK-MGT-RM§#

Table 3.1f: Summary of staff effort (WP Leaders in bold) **(included in Part A)**

Table 3.1g: 'Subcontracting costs' items

1/INSERM		
	Cost (€)	Description of tasks and justification
Subcontracting	117 857	Contribution to Task 1.5: Ethics advisor (42 857€); Contribution to Task 1.4: IPR support (75 000€);
22/EATRIS		
	Cost (€)	Description of tasks and justification
Subcontracting	25 000	Contribution to Task 22.3: Licensing expert for 5 projects (15 000€); IP expert for 5 projects (10 000€);

Table 3.1h: 'Purchase costs' items of participants whose purchase costs exceed 15% of the personnel costs

Please complete the table below for each participant if the purchase costs (i.e. the sum of the costs for 'travel and subsistence', 'equipment', and 'other goods, works and services') exceeds 15% of the personnel costs for that participant (according to the budget table in proposal part A). The record must list cost items in order of costs and starting with the largest cost item, up to the level that the remaining costs are below 15% of personnel costs.

1/INSERM	Cost (€)	Justification
Other goods, works and services	1 371 700	WP1: Future MAB thematic groups (176 700€) WP3: Central budget: costs related to the organisation of the scientific evaluation committees (2/year x 2 calls-JTCs2025/2026) (160 000€) WP8: Central budget: Use case incentives for underrepresented countries (475 000€) WP11: ART-ARNm - consumables and models for PoC studies (T3) (500 000€)
Remaining purchase costs (<15% of pers. Costs)	698 867	
TOTAL	**2 070 567**	
2/TEAMIT	Cost (€)	Justification
Other goods, works and services	368 700	WP2: Communication goods and services Task 2.3. All the communication materials and tools such as videos, infographics, animated infographics, design, website back-end programming and maintenance, podcast, outsourcing engagement events (368 700€)
Remaining purchase costs (<15% of pers. Costs)	7 000	
TOTAL	**375 700**	
3/DLR	Cost (€)	Justification

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Other goods, works and services	80 000	WP3: Task 3.2.2. 2 costs related to the organisation of the scientific evaluation committees JTC2025 (40K€ per meeting) (80 000€)
Remaining purchase costs (<15% of pers. Costs)	24 988	
TOTAL	**104 988**	
4/ANR	Cost (€)	Justification
Other goods, works and services	6 428	WP3: Reimbursement of ethics experts (3 experts per proposal, 100 € per review, 21 proposals) (6428€)
Remaining purchase costs (<15% of pers. Costs)	16 340	
TOTAL	**22 768**	
5/FTELE	Cost (€)	Justification
Other goods, works and services	80 000	WP4: Task 4.2 costs related to the organisation of the scientific evaluation committees of the 1st clinical trial call (80 000€)
Remaining purchase costs (<15% of pers. Costs)	24 150	
TOTAL	**104 150**	
6/LMT	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**9 660**	
8/UT	Cost (€)	Justification
Other goods, works and services	175 000	WP12: Task 12.5 Case study 1 (175 000€)
Remaining purchase costs (<15% of pers. Costs)	181 113	
TOTAL	**356 113**	
13/UKHD	Cost (€)	Justification
Other goods, works and services	413 333	WP9: Cohort data provision - T3 (100 000€) WP10: RS - Longitudinal validation studies PROM (T1) (138 333€) WP12: Task 12.5 Case study 2 (175 000€)
Remaining purchase costs (<15% of pers. Costs)	258 286	
TOTAL	**671 619**	
15/VHIR	Cost (€)	Justification
Other goods, works and services	274 333	WP10: T1 Longitudinal validation studies PROM (138 333€); mHealth adaptation or new creation (100 000€); Meetings (T1) - 2 meetings per use case (36 000€)
Remaining purchase costs (<15% of pers. Costs)	99 286	
TOTAL	**373 619**	
16/LUMC	Cost (€)	Justification
Travel and subsistence	40 000	WP12: Treatment / study design meetings (task 12.2/3)- 2meeting (40000€)
Other goods, works and services	30 000	WP12: Consumables toxicity technician (30000€)
Remaining purchase costs (<15% of pers. Costs)	105 560	
TOTAL	**175 560**	
22/EATRIS	Cost (€)	Justification

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Travel and subsistence	29 600	WP18: Meeting of RDP Regulatory Support Group (including NCA members + EMA representatives) - 2 face to face meetings (M12, M36) (29 600€)
Other goods, works and services	140 000	WP18 IT and web design support for upgrading of the Regulatory Information System (40 000€) WP22: Nonclinical validation steps for selected projects (2 projects @50k each) (100 000€)
Remaining purchase costs (<15% of pers. Costs)	58 793	
TOTAL	**228 393**	
24/APHP	Cost (€)	Justification
Other goods, works and services	138 333	WP10: T1 Longitudinal validation studies PROM (138 333€)
Remaining purchase costs (<15% of pers. Costs)	121 000	
TOTAL	**259 333**	
26/EURORDIS	Cost (€)	Justification
Travel and subsistence	269 100	WP20: Task 20.1: T&S for 25 trainers + 70 trainees + 12 travel fellowships / year (269 100€)
Other goods, works and services	103 800	WP20: Task 20.1.1: Catering + room for 100 people, 3-4 day meeting/year (103 800€)
Remaining purchase costs (<15% of pers. Costs)	47 000	
TOTAL	**419 900**	
27/VULSK	Cost (€)	Justification
Travel and subsistence	30 000	WP24.1 - Knowledges exchanges - 4 meetings Y1 +Y2 (40 persons* 2 meetings) (30000€);
Remaining purchase costs (<15% of pers. Costs)	49 720	
TOTAL	**79 720**	
28/UC	Cost (€)	Justification
Other goods, works and services	227 286	WP21: Consumables/reagents/rodent models for T21.1(20 333€); T21.2.1 (13 000€); T21.2.4 (80 000€); T21.3.1, T21.3.3, T21.3.4 (30 000€); T21.4.2 (30 000€); in vivo work in SCA3 mouse model (15 000€); T21.4.1 (6 000€); T21.5.2 (32 953€) (227 286€)
Remaining purchase costs (<15% of pers. Costs)	7 000	
TOTAL	**234 286**	
29/FFRD	Cost (€)	Justification
Other goods, works and services	285 000	WP25: IRDiRC - One in person CA-SC meeting per year (75K*3) (225 000€); Task Force workshop (20k€/year) (60 000€)
Remaining purchase costs (<15% of pers. Costs)	117 050	
TOTAL	**402 050**	
31/CCUH	Cost (€)	Justification
Travel and subsistence	11 100	WP23 - Travel costs/accommodation costs for the Annual workshop from Y1 to Y3 topic experts - 5 pax per workshop (11100€) Central budget;
Other goods, works and services	35064	WP23 - Catering costs for the Annual 3.2 workshop from Y1 to Y3 (2days event) 64pax (2pax per NMG = 56pax + 3pax WP7 coordination) + 5pax topic experts (35064€) Central budget;
Remaining purchase costs (<15% of pers. Costs)	16 320	

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TOTAL	**62 484**	
34/RDI	Cost (€)	Justification
Other goods, works and services	50 000	WP25: Organisation of the CRN Conference Yr 2 (50 000€);
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**53 000**	
35/ACU	Cost (€)	Justification
Travel and subsistence	3 000	WP1: travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€)
TOTAL	**3 000**	
39/ASU-FC	Cost (€)	Justification
Travel and subsistence	3000	WP1: travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€)
Remaining purchase costs (<15% of pers. Costs)	33 680	
TOTAL	**36 680**	
40/BIU	Cost (€)	Justification
Travel and subsistence	3 000	WP1:Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3 000€)
Other goods, works and services	57 857	WP21: Evaluation of off-target effects ex vivo (GUIDE-Seq, rhAmpSeq) (T21.4.3)
TOTAL	**60 857**	
41/BMBF	Cost (€)	Justification
Travel and subsistence	3 000	WP1:Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3 000€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
TOTAL	**7 000**	
44/CHARITE	Cost (€)	Justification
Other goods, works and services	104 656	WP21: Consumables for T21.2.1, T21.2.2, T21.2.4 (40 656€); Consumables for T21.3 (10 000€); Consumables for T21.5.1, T21.5.2 and T21.5.4 (54 000€);
Remaining purchase costs (<15% of pers. Costs)	20 829	
TOTAL	**125 485**	
45/CHI	Cost (€)	Justification
Other goods, works and services	80 571	WP21: Consumables for: 3,000€ for multiligand assays and 47,571€ for multiomics single cell analyses (T.21.5.1), 10,000€ for analysis of humanized NSG mice exposed to tools T21.1-T21.4 (T.21.5.2), 20,000€ qualification of single cell platform (T.21.5.3) (80571€);
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**83 571**	
52/ELS	Cost (€)	Justification
Travel and subsistence	3 000	WP1:Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3 000€)
Other goods, works and services	333 960	WP1.3: Elsevier Licence (333 960€)
TOTAL	**336 960**	
53/Erasmus MC	Cost (€)	Justification
Other goods, works and services	174 333	WP10.2 WP10.3: T1 Longitudinal validation studies PROM (138 333€); Meetings (T1) - 2 meetings per use case (36 000€)

Remaining purchase costs (<15% of pers. Costs)	40 000	
TOTAL	**214 333**	
54/F.R.S.-FNRS	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**9 660**	
55/FHG	Cost (€)	Justification
Other goods, works and services	116 428	WP21: Consumables/reagents for analytics (T21.1.1, T21.1.2) (50 428€); for T21.2.3 (50,000€) and T21.2.5 (12 000€) (62 000€) and for T21.3 (4 000€)
Remaining purchase costs (<15% of pers. Costs)	23 159	
TOTAL	**139 587**	
56/FRRB	Cost (€)	Justification
Travel and subsistence	9 660	WP1 : JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
TOTAL	**13 660**	
57/ECRIN	Cost (€)	Justification
Travel and subsistence	8 600	WP20.3.4: travels and accommodation for 8 trainers/staff for 2-3 days /year + 2 fellowships/year (8600€);
Other goods, works and services	3 180	WP20.3.4. Catering costs: 30 people, 2 to 3-day meeting / year (3180€);
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**14 780**	
58/FWF	Cost (€)	Justification
Travel and subsistence	7 440	WP1 : Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**13 660**	
59/ IFD	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
Remaining purchase costs (<15% of pers. Costs)	740	
TOTAL	**12 180**	
61/FCT	Cost (€)	Justification

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Travel and subsistence	9 660	WP1 : JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
TOTAL	**9 660**	
62/MZd	Cost (€)	Justification
Other goods, works and services	4 000	Audit costs (4000€)
TOTAL	**4 000**	
62.1 AZV	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Remaining purchase costs (<15% of pers. Costs)	740	
TOTAL	**8 180**	
63/GNT	Cost (€)	Justification
Other goods, works and services	99 214	WP21: 65,214€ for consumables and reagents for viral vector production and characterization (T21.1.1) and for QC testing (T21.1.2); 34,000€ for in vitro editing of DMD myoblasts (Cas 9, base editors, molecular biology) (T21.4.1) and for in vivo editing in DMD mouse model, plus analysis of off target effect in vivo (AAV Cas9 and base editing, molecular biology and histology) (T21.4.2)
Remaining purchase costs (<15% of pers. Costs)	18 000	
TOTAL	**117 214**	
67/HRB	Cost (€)	Justification
Travel and subsistence	4 440	WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Remaining purchase costs (<15% of pers. Costs)	18 100	
TOTAL	**22 540**	
69/Rannis	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**9 660**	
70/IMAGINE	Cost (€)	Justification
Other goods, works and services	40 714	WP21: Consumables - Molecular and cellular biology reagents (including DNA/RNA synthesis, antibodies, Tissue culture supplies and transfection reagents), mouse experiments and laboratory disposables (T21.4.1 and T21.4.2) (40714€);
Remaining purchase costs (<15% of pers. Costs)	20 093	
TOTAL	**60 807**	
73/INSA	Cost (€)	Justification
Travel and subsistence	4 440	WP23: Travel costs/accomodation costs for the Annual workshop from Y1 to Y7 - 2 pax per workshop - NMG Portugal (4440€)
Remaining purchase costs (<15% of pers. Costs)	7 440	

TOTAL	**11 880**	
74/IOR	Cost (€)	Justification
Travel and subsistence	3 000	WP1:Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3 000€)
Other goods, works and services	3 500	WP25: ERN meeting Year 3 (3500€)
TOTAL	**6 500**	
75/ISS	Cost (€)	Justification
Travel and subsistence	34 400	WP20.3.5: travels and accommodation for 8 trainers/staff for 2-3 days /year + 2 fellowships/year (25800€); WP14: 1xBYOD hackathon (travel/accommodation of 10 participants) (8600€);
Other goods, works and services	9 540	WP20: task 20.3.5. Catering costs: 30 people, 2 to 3-day meeting / year (9540€);
Remaining purchase costs (<15% of pers. Costs)	9 260	
TOTAL	**53 200**	
76/IT-MOH	Cost (€)	Justification
Travel and subsistence	9 660	WP1 : JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
TOTAL	**13 660**	
77/KU Leuven	Cost (€)	Justification
Other goods, works and services	83 978	WP21: consumables (so reagents, materials and plastics) associated to T21.1 (83978€);
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**86 978**	
78/LZP	Cost (€)	Justification
Travel and subsistence	9 660	WP1 : JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
TOTAL	**9 660**	
82/MUR	Cost (€)	Justification
Travel and subsistence	9 660	WP1 : JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
TOTAL	**13 660**	
83/NCBR	Cost (€)	Justification
Travel and subsistence	9 660	WP1 : JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
TOTAL	**13 660**	

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85/MoH SR	Cost (€)	Justification
Travel and subsistence	3 000	WP1: travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€)
Remaining purchase costs (<15% of pers. Costs)	8 880	
TOTAL	**11 880**	
86/RDG	Cost (€)	Justification
Travel and subsistence	4 440	WP23: Travel costs/accomodation costs for the Annual general meeting from Y1 to Y3 2 pax per meeting - NMG (4440€)
Remaining purchase costs (<15% of pers. Costs)	7 440	
TOTAL	**11 880**	
89/OSR	Cost (€)	Justification
Other goods, works and services	311 314	WP21: Mouse experiments and laboratory disposable (T.21.4.2) (158 314€); 50,000€ for consumables: Molecular and cellular biology reagents (including DNA/RNA synthesis, antibodies, Tissue culture supplies and transfection reagents) (T21.4.1); 30,000€ for mouse experiments, in vivo GE barcoding, LiBiSseq and SLIM PCR (T21.4.3); 73,000€ for consumables for multiparameter flow cytometry, generation of Ag-specific cell lines (T.21.5.1), Generation of specific Treg and PoC specific Treg in vitro and in vivo (humanized mice) (T21.5.4)"
Remaining purchase costs (<15% of pers. Costs)	7 000	
TOTAL	**318 314**	
90/JSI	Cost (€)	Justification
Travel and subsistence	8 880	WP23: Travel costs/accomodation costs for the Annual general meeting from Y1 to Y3 2 pax per meeting - NMG (4440€) ; Travel costs/accomodation costs for the Annual workshop from Y1 to Y7 - 2 pax per workshop - NMG (4440€)
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**11 880**	
91/RCN	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**13 660**	
92/FWO	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**13 660**	
93/REUH	Cost (€)	Justification
Travel and subsistence	30 000	WP24.1 - Knowledges exchanges - 4 meetings Y1 +Y2 (40 persons* 2 meetings) (30000€);

Remaining purchase costs (<15% of pers. Costs)	4 660	
TOTAL	**34 660**	
94/RIF	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**13 660**	
98/SPW	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**13 660**	
100/ETAg	Cost (€)	Justification
Travel and subsistence	9 660	WP1: JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
TOTAL	**9 660**	
101/SAS	Cost (€)	Justification
Travel and subsistence	9 660	WP1: JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
TOTAL	**9 660**	
103/MOSAE	Cost (€)	Justification
Travel and subsistence	9 660	WP1: JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
TOTAL	**9 660**	
104/SRC	Cost (€)	Justification
Travel and subsistence	9 660	WP1: JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
TOTAL	**13 660**	
105/TEDDY	Cost (€)	Justification
Travel and subsistence	15 440	WP20: task 20.1.2: travels and accommodation for 10 trainers and staff / year + 3 travel fellowships per year (1 edition) (11180€);: catering costs for 20 people for 2 day-meeting (1 edition) (4260€);

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Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**18 440**	
107/TIF	Cost (€)	Justification
Travel and subsistence	8 880	WP23: Travel costs/accomodation costs for the Annual workshop from Y1 to Y3 - 2 pax per workshop - NMG Cyprus (4440€) ; Travel costs/accomodation costs for the Annual general meeting from Y1 to Y3 2 pax per meeting - NMG Cyprus (4440€)
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**11 880**	
108/TUBITAK	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**13 660**	
109/RT (TuscReg)	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**9 660**	
110/UAB	Cost (€)	Justification
Other goods, works and services	19 286	WP21: Plastic ware and reagents for viral vector production and characterization (T21.1.1), Taqman qPCR reagents to quantify the vector yield in each production. Consumables for analytics (T21.1.2) (19286€);
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**22 286**	
112/UCSC	Cost (€)	Justification
Travel and subsistence	7 500	WP20: Task 20.4 - Accommodation & Travel costs for 5 fellows (7500€);
Other goods, works and services	9 000	WP20: Task 20.4. classrooms and wrap meeting costs (9000€);
Remaining purchase costs (<15% of pers. Costs)	10 400	
TOTAL	**26 900**	
113/UEF	Cost (€)	Justification
Other goods, works and services	52 800	WP21: 6,000€ consumables (T21.2.1), 30,000€ consumables (T21.2.2), 15,000€ consumables for in vitro and in vivo (T21.2.4); 1,800€ consumables for T21.3 (52800€);
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**55 800**	
115/UKLFR	Cost (€)	Justification
Other goods, works and services	48 571	WP21: 48,571€ Evaluation of off-target effects in vivo (CAST-Seq, rhAmpSeq, long-read seq) (T21.4.3)

Remaining purchase costs (<15% of pers. Costs)	26 000	
TOTAL	**74 571**	
122/c4c-S	Cost (€)	Justification
Travel and subsistence	11 180	WP20: task 20.1.2: travels and accommodation for 10 trainers and staff / year + 3 travel fellowships per year (1 edition) (11180€);
Remaining purchase costs (<15% of pers. Costs)	7 260	
TOTAL	**18 440**	
124/CNRS	Cost (€)	Justification
Other goods, works and services	37 714	WP21: For consumables for understanding of current LNPs/EVs/NPs in T.21.3.1, evaluation of efficacy T.21.3.3, AI tools development (T.21.3.2), demonstration of scalability in T.21.3.4, and regulatory challenges with EV and biohybrids encapsulating mRNA (T21.3.6) (37714€);
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**40 714**	
125/CIBER	Cost (€)	Justification
Other goods, works and services	81 969	WP21: 37,969€ consumables for targeting to hematopoietic stem cells, PBMC subsets, CNS and liver (T21.3.1), and in vitro and in vivo evaluation of efficacy, immunogenicity and safety of mRNA formulations (T21.3.3); 44,000€: 20,000€ for mouse experiments and laboratory disposables (T21.4.2), 24,000 for consumables: Molecular and cellular biology reagents (including DNA/RNA synthesis, antibodies, Tissue culture supplies and transfection reagents) (T21.4.1)
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**84 969**	
126/UEFISCDI	Cost (€)	Justification
Travel and subsistence	9 660	WP1 : JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Other goods, works and services	4 000	WP1: Audit Costs (4000€)
TOTAL	**13 660**	
129/BNSF	Cost (€)	Justification
Travel and subsistence	9 660	WP1: JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
TOTAL	**9 660**	
136.1/KUM	Cost (€)	Justification
Other goods, works and services	204 333	WP10: T1 Longitudinal validation studies PROM (138 333€); Meetings organisation (T1) - 2 meetings per use case (36 000€); other goods and services T1 PAO reimbursement (10.000€ per year per use case) (30 000€)
Remaining purchase costs (<15% of pers. Costs)	34 500	
TOTAL	**238 833**	
138/FNR	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)

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Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**9 660**	
139/NKFIH	Cost (€)	Justification
Travel and subsistence	9 660	WP1: JTC CSC travel to monitoring meetings (3 meetings x740€) (2220€); Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
TOTAL	**9 660**	
140/PEI	Cost (€)	Justification
Other goods, works and services	37 705	WP21: Consumables for setting up and validating quality assays on AAV vector stocks (Task 21.1), Consumables for T21.2, Consumables for T21.3 (37 705) ;
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**40 705**	
141/PLUS	Cost (€)	Justification
Other goods, works and services	52 000	WP21: For understanding of current LNPs/EVs/NPs in T21.3.1 (52000€)
Remaining purchase costs (<15% of pers. Costs)	5 250	
TOTAL	**57 250**	
142/SU	Cost (€)	Justification
Travel and subsistence	3 000	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€)
TOTAL	**3 000**	
144/Vinnova	Cost (€)	Justification
Travel and subsistence	7 440	WP1: Travel to 3 consortium meetings (1 pax per partner/1000€ per travel) (3000€) WP3: Travel costs to 6 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (4440€)
Remaining purchase costs (<15% of pers. Costs)	2 220	
TOTAL	**9 660**	
149/UO	Cost (€)	Justification
Travel and subsistence	8 880	WP23 Travel costs/accommodation costs for the Annual general meeting from Y1 to Y3 2 pax per meeting - NMG (4440€) ; Travel costs/accommodation costs for the Annual workshop from Y1 to Y7 - 2 pax per workshop - NMG (4440€)
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**11 880**	

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Table 3.1i: 'Other costs categories' items (e.g. internally invoiced goods and services)

1/INSERM		
	Cost (€)	Justification
Internally invoiced goods and services	10 286	WP21: 1,000€ for Cas9 immunogenicity in rodent models (T21.5.4) 9,286€ for Rodent models to mimic adaptive immune response (T21.5.2)
70/IMAGINE		
	Cost (€)	Justification
Internally invoiced goods and services	4 286	WP21: Use of the Imagine core facilities (i.e., genomics, bioinformatics, flow cytometry and mouse facilities) (T21.4.1 & T21.4.2)

4/ANR		
	Cost (€)	Justification
Financial support to third parties	12 857 143 €	3 JTCs (12 857 143€)
5/FTELE		
	Cost (€)	Justification
Financial support to third parties	3 000 000 €	3 JTCs (3 000 000€)
6/LMT		
	Cost (€)	Justification
Financial support to third parties	428 571 €	3 JTCs (428 571€)
7/ZonMw		
	Cost (€)	Justification
Financial support to third parties	5 400 000 €	2 JTCs (3 600 000€) funding of PAO (500 000€ per call) Networking Support Scheme (800 000€)
29/FFRD		
	Cost (€)	Justification
Financial support to third parties	300 000 €	3 JTCs (300 000€)
41/BMBF		
	Cost (€)	Justification
Financial support to third parties	9 000 000 €	3 JTCs (3 000 000€ per call)
49/CSO-MOH		
	Cost (€)	Justification
Financial support to third parties	960 000 €	3 JTCs (320 000€ per call)
54/F.R.S.-FNRS		
	Cost (€)	Justification
Financial support to third parties	900 000 €	3 JTCs (300 000€ per call)
56/FRRB		
	Cost (€)	Justification
Financial support to third parties	4 500 000 €	3 JTCs (4 500 000€)
58/FWF		
	Cost (€)	Justification
Financial support to third parties	2 700 000 €	3 JTCs (900 000€ per call)
59/IFD		

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	Cost (€)	Justification
Financial support to third parties	3 000 000 €	3 JTCs (1 000 000€ per call)
61/FCT		
	Cost (€)	Justification
Financial support to third parties	1 050 000 €	3 JTCs (1 050 000€)
62/MZd		
	Cost (€)	Justification
Financial support to third parties	1 500 000	3 JTCs (1 500 000€)
67/HRB		
	Cost (€)	Justification
Financial support to third parties	1 500 000 €	3 JTCs (1 500 000€)
69/Rannis		
	Cost (€)	Justification
Financial support to third parties	428 571 €	3 JTCs (428 571€)
72/ISCIII		
	Cost (€)	Justification
Financial support to third parties	4 800 000 €	3 JTCs (4 800 000€)
76/IT/MOH		
	Cost (€)	Justification
Financial support to third parties	3 000 000 €	3 JTCs (3 000 000€)
78/LZP		
	Cost (€)	Justification
Financial support to third parties	300 000 €	3 JTCs (300 000€)
82/MUR		
	Cost (€)	Justification
Financial support to third parties	3 000 000 €	3 JTCs (3 000 000€)
83/NCBR		
	Cost (€)	Justification
Financial support to third parties	3 600 000 €	3 JTCs (1 200 000€ per call)
91/RCN		
	Cost (€)	Justification
Financial support to third parties	1 542 857 €	3 JTCs (1 542 857€)
92/FWO		
	Cost (€)	Justification
Financial support to third parties	2 100 000 €	3 JTCs (700 000€ per call)
94/RIF		
	Cost (€)	Justification
Financial support to third parties	3 000 000 €	JTCs (3 000 000€)
98/SPW		
	Cost (€)	Justification

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Financial support to third parties	3 000 000 €	3 JTCs (1Mio€ per call)
100/ETAg		
	Cost (€)	Justification
Financial support to third parties	150 000 €	1 JTC (150 000€)
101/SAS		
	Cost (€)	Justification
Financial support to third parties	120 000 €	1 JTC (120 000€)
103/MOSAE		
	Cost (€)	Justification
Financial support to third parties	150 000 €	1 JTC (150 000€)
104/SRC		
	Cost (€)	Justification
Financial support to third parties	1 457 143 €	3 JTCs (1 457 143€)
108/TUBITAK		
	Cost (€)	Justification
Financial support to third parties	1 500 000 €	3 JTCs (500 000€ per call)
109/RT (TuscReg)		
	Cost (€)	Justification
Financial support to third parties	900 000 €	3 JTCs (900 000€)
126/UEFISCDI		
	Cost (€)	Justification
Financial support to third parties	3 000 000 €	3 JTCs (3 000 000€)
129/BNSF		
	Cost (€)	Justification
Financial support to third parties	225 000 €	3 JTCs (225 000€)
138/FNR		
	Cost (€)	Justification
Financial support to third parties	990 000 €	3 JTCs (330 000€ per call)
139/NKFIH		
	Cost (€)	Justification
Financial support to third parties	900 000 €	3 JTCs (300 000€ per call)
144/Vinnova		
	Cost (€)	Justification
Financial support to third parties	1 414 286 €	3 JTCs (1414286€)
152/CIHR*		
	Cost (€)	Justification
Financial support to third parties	2 808 000€	3 JTCs ($1 050 000 per call) -Ass. Part. not receiving EC funding
153/DFG*		
	Cost (€)	Justification

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Financial support to third parties	5 400 000€	3 JTCs (1 800 000€)-Ass. Part. not receiving EC funding
155/FRQS*		
	Cost (€)	Justification
Financial support to third parties	350 000€	1JTC (350 000€)-Ass. Part. not receiving EC funding
165/SNSF*		
	Cost (€)	Justification
Financial support to third parties	2 000 000€	2 JTCs (2 000 000€)-Ass. Part. not receiving EC funding

Table 3.1j: 'In-kind contributions' provided by third parties

89 - OSR			
Third party name	**Category**	**Cost (€)**	**Justification**
Università Vita-Salute San Raffaele (UniSR)	Seconded personnel	46 137€	Art 9.2 eligible in kind for free: WP21
37-AMU			
Third party name	**Category**	**Cost (€)**	**Justification**
Protisvalor Mediterranée SAS (PVM)	Personnel	0.00€	The partner Aix-Marseille Université (AMU) will receive the support of Protisvalor Mediterranée SAS (PVM). Protisvalor Mediterranée SAS (PVM), a spin-off company created by AMU to handle the financial and administrative aspects of AMU's projects. Protisvalor will act as In-kind contributors against payments of AMU. PVM is linked to AMU through a Framework Agreement validated by the French Ministry of Research and Higher Education (MESR), giving the right for PVM to administer. In H2020, PVM was involved in 116 projects whereas in HEUR PVM is involved until now in 53 projects. Consequently, PROTISVALOR will manage the administrative and financial aspects on behalf of AMU in the ERDERA project. The department will handle some means and expenses necessary for the fulfillment of the objectives of the project, e.g., purchasing necessary consumables and/or equipment; handling dissemination and publication costs; and any other necessary project expenses. All expenses incurred by PVM will be recorded in its own accounts and reported in the AMU financial report.

#§QUA-LIT-QL§# #§WRK-PLA-WP§#

3.2. Capacity of participants and consortium as a whole #@CON-SOR-CS@# #@PRJ-MGT-PM@#

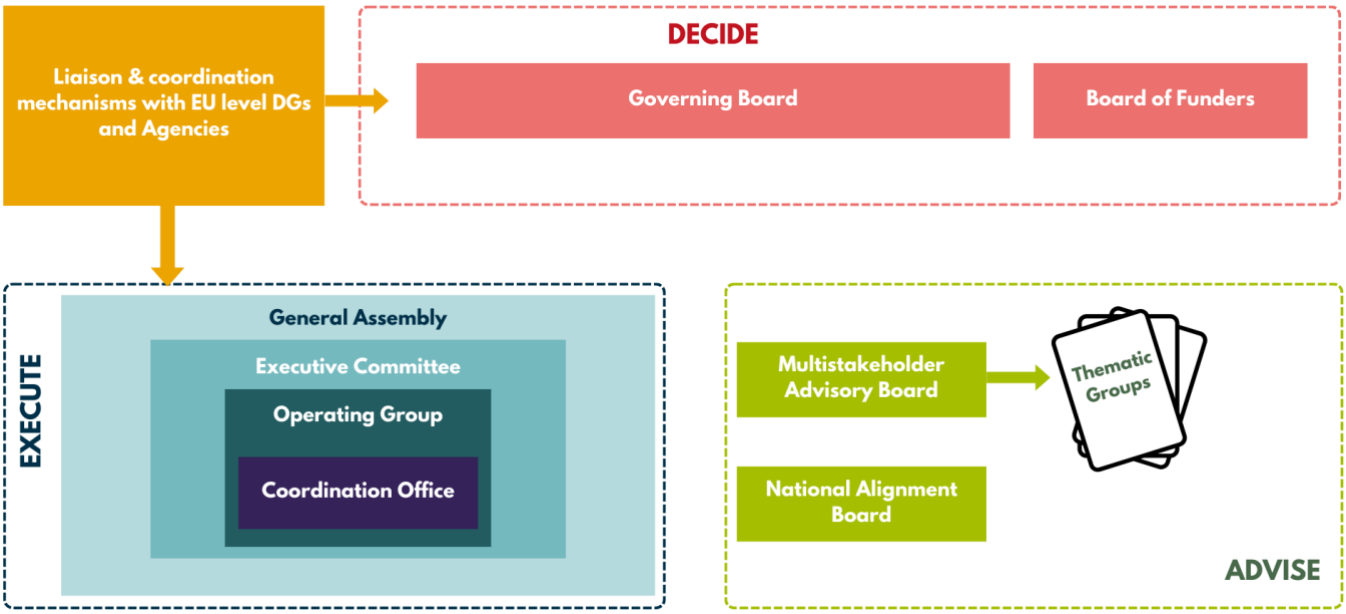
The details on how ERDERA's consortium will tackle project's objectives, contribute to societal impacts, encompass meaningful collaborations with MS/ACs and expand to other networks and initiatives, are described in detail in the proposal sections 1 (Excellence) and 2 (Impact). However, it is important to underline that **ERDERA brings together** a broad consortium of **key actors and stakeholders representing the whole rare diseases ecosystem** and thus guaranteeing integrity of the pipeline. The Alliance is composed of 171 organisations (152 Beneficiaries and 19 Associated Partners) from 26 European countries (AT, BE, BG, CY, CZ, DE, DK, EE, ES, FI, FR, GR, HU, IE, IT, LV, LT, LU, NL, PL, PT, RO, RS, SE, SK, SI), 7 associated countries (GE, IS, IL, MA, NO,TR, UK) and 3 non-EU country (AU, CA, CH) bringing together complementary knowledge, infrastructures and expertise necessary to fulfil the set aims. 38 funders, 115 research performing organisations, 12 patient organisations, 3 research infrastructures and 27 private for-profit organisations (industry & SMEs) are part of the consortium. Even though many of ERDERA's partners have participated in the EJP RD programme, the consortium

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importantly expands towards a more complete representation of the RD ecosystem by including industry members (6 large pharmaceutical companies, as Associated Partners), more patient organisations (12) to better capture the voice of patients and target underserved rare diseases and new research funding (38) and research performing organisations (115). Globally, there is an important expansion in the number of entities involved (from 93 in EJP RD to 171 in ERDERA) which notably enhances the activities to be undertaken and their impact. Moreover, the majority of ERDERA partners have existing collaborations established through previous projects or are united within existing (infra)structures.

As demonstrated in the Methodology sub-chapter, although crucial, the joint transnational calls and resulting research projects are only one of the building blocks of ERDERA. Beyond the planned funding opportunities, the Partnership will undertake a comprehensive and solid R&D programme, organised in 25 WPs and 7 overarching Workstreams tightly interlinked to ensure a smooth connection and mutual benefit between funding activities and the rest of the programme. A strong linkage to national priorities and capacities will be enabled in ERDERA via the creation of National Mirror Groups (WP23), the National Alignment Board foreseen in the governance and the national commitments in terms of funding (167.5 M€ earmarked). The Clinical Research Network, including its Diagnostics Pole and the connection with expertise, education and data capacities will further support the national alignment and exploit national capacities. RDs posing health and societal challenges at global level, ERDERA will take advantage of international expertise by directly involving or engaging with partners from outside of Europe (e.g. Canada, Australia) and of international nature (Rare Diseases International [RDI], World Duchenne Organisation [WDO], International Rare Diseases Research Consortium [IRDiRC]) to jointly tackle overarching RD issues, strengthen knowledge sharing and common solutions.

3.2.1 Governance

ERDERA is an ambitious initiative aiming at establishing an impactful and sustainable structure as part of the RD ecosystem. Accordingly, it will establish a clear governance in order to meet its objectives, build trust and encompass interests of participating parties and efficiently solve potential conflicts. The ERDERA management structure aims at transparent decision-making, implementation and advisory processes with well-defined responsibilities. It will set up an adaptive structure able to tackle emerging needs and opportunities. It will manage the strategy planning, annual work (plans) and allocation of resources. Moreover, it will be responsible for interactions with external stakeholders. The proposed organizational structure of the ERDERA is depicted in the figure below:



Governing Board

The **Governing Board** and the Board of Funders will operate at the decision-making level. The **Governing Board** (GB) will be composed by

(i) one representative of each participating EU Member State, Associated Countries and Third countries

and one member representing each of the following stakeholder groups:

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(ii) Patients;
(iii) EU Research Infrastructures;
(iv) Industry;
(v) ERNs;
(vi) EC Representatives.

The representative(s) of the European Commission's policy responsible service (DG Research & Innovation, DG RTD) will sit at the GB with an observer status.
National representatives to the GB:
One Principal Representative and one Permanent Deputy shall be nominated for each participating country. Nominated Principal Representatives and their Permanent Deputies shall not be members of other ERDERA bodies. Exceptions may apply for certain countries with limited human resources. Members of the GB will actively participate in a cooperative manner in the activities and meetings of the GB.
The GB will select a chair and vice-chair, one of them from an under-represented country, who will represent the voice and the quorum decisions of the GB. The ERDERA coordination office will ensure the secretarial support to the GB. All GB meetings will be co-moderated by the GB chair and the ERDERA coordinator. When relevant, the GB chair and vice-chair will also support the coordinator to enhance the political and strategic visibility of the programme.
The GB is the ultimate decision-making body regarding any strategic decisions of ERDERA, excluding final decisions on topics of joint transnational calls, which fall under the mandate of the Board of Funders. More specifically, the GB:

- provides the strategic steering and ensures coherence, between Partnership activities and relevant European/national/international initiatives and policies;
- provides feedback and approves ERDERA priorities (and sensitive strategic matters) through the rolling annual plans;
- delivers input to the ERDERA progression (periodic reports, AWP) and provide feedback to key strategic milestones/deliverables;
- contributes to facilitate the uptake of the ERDERA results and outcomes and catalyses the exchanges of best practices and their uptake at the National level;
- reflects on sustainability of ERDERA outcomes and research resources.

The GB will provide feedback, discuss and approve the strategic propositions made by the Executive Committee (ExCom) and the General Assembly (GA). In particular, the GB will provide feedback and approve: (i) the initial SRIA and its updates; (ii) the inclusion and exclusion of partners; (iii) the AWPs and annual summary reports; (iv) the achievement of the most significant milestones; (v) the budget; (vi) the ethical, legal and data management frameworks; (vii) and the ERDERA long-term sustainability plan. As a result, budgets and workplans are subject to change based on the outputs of the programme monitoring activities, followed by discussion and approval of AWPs. The GB will meet twice per year and *ad hoc* meetings may be organised whenever it is necessary to discuss strategic orientations of ERDERA. One of the yearly meetings will be face-to-face for the approval of the AWP and may be combined with a meeting of the ExCom and MAB. The second yearly meeting will be virtual. A structured process will be put in place, to facilitate GB in providing feedback and allow sufficient time to provide input, discuss and take informed decisions, as a separate decision-making body.
The **Board of Funders (BoF)** will be composed by one representative per Research Funding Organisation. It will be chaired by the leader of the RD Funding Work Stream and co-chaired by a representative from under-represented country. The EC will be a member of the Board of Funders. The BoF will be the ultimate decision maker with regards to ERDERA's competitive calls for projects. This comprises the design of the call, timelines, call texts and topics, guidelines and rules for participation and topics selection. For JTCs based on a 2-step evaluation process and recommendation by the JTC Scientific Evaluation Committee, the BoF has final decision on the pre-proposals to be invited to the second stage and on the final list of projects to be funded. Each BoF's organisation makes the final decision on its funding contribution according to its respective regulations, calendar and legal frameworks, but commits to follow the list of projects recommended for funding and prioritized by the BoF. The BoF will also supervise the progress of the calls

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and the evaluation of proposals, and monitor actions taken by the acting Call Secretariat. It will validate the composition of the respective JTC Scientific Evaluation Committees and ensure the correct implementation of procedures. The BoF will meet at least twice a year.

The execution of ERDERA's activities will rely on the **General Assembly, Executive Committee, Operating Group and Coordination Office**. The General Assembly (GA) will meet once a year and will manage the contractual implementation of ERDERA on the scientific and administrative level. It will be composed by one member per consortium organisation, including Grant Agreement Signatories and Associated Partners, divided in 4 stakeholder groups: (i) Funders; (ii) Research performing organisations receiving funding (RPO); patient representatives (iii) Industry members (providing in-kind contributions and engaged as Associated Partners).

General Assembly

The GA will manage the contractual implementation of ERDERA on the scientific and administrative level. GA will also have an important role in developing proposals for the scientific priorities and strategic orientations to be submitted for feedback, discussion and final approval by the GB.

GA will develop proposals and preparatory agreements for any substantial and strategic decisions requiring the contribution of the whole consortium. In particular, the GA will submit proposals for feedback, discussion and final approval decision of the Governing Board regarding: (i) the initial SRIA and its updates; (ii) invitation or removal of members from the consortium; (iii) the Annual Work Plans and annual summary reports; (iv) the achievement of the most significant milestones and deliverables; (v) the ethical, legal and data management frameworks developed; (vi) the long-term sustainability plan for ERDERA.

Executive Committee

The **Executive Committee** (ExCom) will consist of the Coordination Team, Work Stream Leaders and all WP Leaders, chaired by the Coordinator. ExCom will ensure the implementation of ERDERA's actions according to the overall 7-year plan and the individual AWPs, monitoring progress according to the milestones set out. The ExCom will develop the AWPs and be responsible for the quality control of deliverables and reports. It will adopt solutions to problems encountered during implementation. The ExCom shall refer to and get approval from the GA and GB if no agreement is reached or if the solution implies major deviations from the work plans agreed by the GB. Whenever the problems encountered may impact the future EU and/or Member States research strategy issues, then such issues should be discussed proactively and seek approval of the GB and the EC services. The Coordinator will duly inform the relevant bodies (GA, GB, MAB) to prepare the discussion and, where relevant, the approval of the GB/EC about expected deviations. Additionally, ExCom will oversee how resources are spent and propose changes if needed. It will support the GA in preparing the basis for decisions to be taken by the GB. Moreover, it will support the establishment of connections with sister initiatives at national, EU and international level. The ExCom will meet every three months.

Since the ExCom will be a relatively large body, an **Operating Group (OG)** will be created for the efficient administration of day-to-day activities. The Operating Group will be composed of the Coordination Team and all Work Stream leaders. The OG will be responsible for close communication and coordination of activities between different Work Streams and WPs, reflecting on progress and future direction and vision for ERDERA. Regular conference calls will ensure close follow up of activities, continuous alignment and adequate reactivity in case of urgent situations requiring risk management. The OG will participate in the preparation of the ExCom meetings and support the development of the Annual Work Plans. It will meet every three weeks.

The **Coordination Office** will be composed by the Coordinator (Coo) and the Coordination Team (Coo Team). It will be under the responsibility of the Coordinator and will include a team of managers with expertise in project management, communication, financial and administrative aspects, risk management, ethics, patient engagement, data management, legal, sustainability, impact and monitoring. The Coo, supported by the Coordination Office, will be in charge of the day- to-day overall scientific, administrative and financial management of the project and will be the primary contact point for the European Commission. Moreover, the Coo will represent ERDERA at the EU and international level. The Coordination Office will: (i) ensure the implementation of the Grant Agreement signed with the EC; (ii) prepare the Consortium Agreement (CA) to be signed by the consortium; (iii) update the CA and submit amendment requests to the Grant Agreement; (iv) oversee deadlines of milestones and activities and quality control of deliverables; (v) propose contingency action plans to the ExCom and oversee their

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implementation; (vi) report on the implementation of the initiative and challenges encountered to the ExCom; (vii) act as the scientific secretariat of the ExCom meetings; (viii) facilitate cooperation and alignment across WPs and Work Streams; (ix) ensure technical and financial reporting to the European Commission and budget management; (x) organise the GB and MAB meetings; (xi) ensure transversal activities (coordination, management, communication, strategy, sustainability, ethics); (xii) follow-up on the impact and monitoring of ERDERA; (xiii) Implement the engagement strategy of the Partnership proposed by the ExCom, developed in collaboration with MAB and the National Alignment Board and validated by the GB. Meetings of the Coordination Office will be called every 2 weeks. The advisory level will consist of the Multistakeholder Advisory Board and the National Alignment Board.

A permanent Multistakeholder Advisory Board (MAB) will be established to allow a good overview of the ERDERA progress and allow informed advice. MAB will be composed of external independent experts representing different types of stakeholder perspectives (i.e., patient organisations, academic institutions, public and private funders, regulatory bodies, including EMA, FDA and Health Technology Assessment (HTA) representatives at the EU level (e.g., EU-Innovation Network), EHDS representatives, ERN representatives, ethicists, etc). The final list of experts that will compose the MAB will be included as a deliverable. The MAB will support the consortium and the GB by providing key advice to feed the strategy of the research and support activities foreseen in ERDERA. This may include advice on the future orientations of the Clinical Research Network, Joint Transnational Calls and Clinical Trial Calls, the exploitation strategies of research results etc. In addition, MAB will ensure that patient needs are key drivers for funded research and support activities and focus is on priorities that maximise the impact of the partnership, targeting under-represented diseases, meaningful topics yet underexplored, and guaranteeing high-quality, open and re-usable results and translation in clinical impact.

The MAB may suggest the creation of temporary or permanent thematic groups involving additional external experts to expand the expertise of the MAB and advise ERDERA's partners on specific matters, such as the ones mentioned above. These expert groups will always include some MAB members and will be chaired by one of the MAB permanent experts. The MAB will meet every four months.

The **National Alignment Board** (NAB) will be composed of representatives of each National Mirror Group (NMG) and representatives of the European Commission services when relevant. NAB will have a Chair and a vice-chair, one of them being from an underrepresented country and will report regularly to GB, particularly on implementation of best practices. European networks of relevance, with national representations (such as ERN Board of Member States, HTA network etc.) could possibly be involved too, to support national alignment and efforts.

The chair of the NAB will update the GB and the MAB on the NAB discussions and activities. The NAB will provide continuous feedback from relevant national stakeholders in order to translate efficiently the specific needs and strategy represented by countries or European Commission as well as the outcomes of ERDERA. Thus, the NAB will ensure that national activities, strategies and needs are considered when taking decisions at the Partnership level and when designing the AWPs. NAB meetings will take place at least once a year in order to share the progress on the creation and operations of NMGs, to highlight success stories and to share good practices. As described above and shown in the governance figure, the European Commission will have a strong voice in the ERDERA partnership through several mechanisms: member of the Governing Board and the Funders Board and via regular liaison with the Executive bodies in the governance. In addition to this direct representation, the interaction will be enrolled through regular meetings between the Coo and the EC Directorate Generals and relevant Agencies to ensure appropriate liaison & coordination.

Conflicts of interest:

The rules applied under Horizon Europe for Conflict of Interest will be applied whenever such conflict may impact the functioning of the governing or advisory bodies. A Conflict of Interest (CoI) is a situation where the impartial and objective involvement is compromised for reasons involving economic interest, political or national affinity, family or emotional ties or any other shared interest.

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While the execution part will involve mostly the Coordination team, OG, ExCom, and General Assembly, the governance will be structured around the GB and the Board of Funders. The first one will provide the political and strategic steering within the frame of the Partnership to ensure coherence between Partnership activities and relevant European/national/international policies and priorities and facilitate the uptake of the Partnership results and outcomes and reflect on sustainability. The latter has a specific and "limited" role in the context of funding activities of the Partnership that are based on the provision of funding to third parties (Joint Transnational Calls, Networking support scheme and Clinical Trials Call). The strategic process will involve additionally the MAB and the National Alignment Board.
To keep the Partnership on track while acknowledging the flexibility necessary to adapt its strategy to the evolving scientific and policy circumstances and to allow on timely deployment of revised agendas and activities, the governance and strategy driving processes must be dynamic and agile. This requires implementation of clear processes, tools and regular meetings to support the work of governing and strategy bodies.

A structured and collaborative process will be implemented to ensure that the SRIA remains relevant, aligned with changing goals and priorities, and responsive to emerging challenges and opportunities. Stakeholders including, but not limited to researchers, patient representatives, policymakers, industry representatives and relevant experts will remain engaged in the SRIA Task Force and aligned through the organization of workshops, focus groups, and surveys to gather input on the current SRIA's strengths, weaknesses, and areas for improvement. The alignment with national, regional, and international research and innovation policies and strategies will continuously be sought with the help of the Governing Board.
A comprehensive analysis of the changing technological, economic, social, and environmental landscape will be conducted as part of the environmental scan, with the help of the MAB. It will seek to identifying emerging trends, challenges, and opportunities that may impact the SRIA's relevance and effectiveness. The SRIA will also undergo a SWOT analysis to identify gaps or shortcomings in the existing agenda that need to be addressed.
The review of previous performance will be accomplished through the assessment of the progress made on the goals and objectives outlined in the current SRIA version, using the ERDERA monitoring framework, identifying areas where targets were met, exceeded, or fell short.
Considering the insights from the above-described stakeholder engagement, environmental scan, and SWOT analysis, objectives may be added or updated to be made clearer and more measurable, and priorities would be defined based on the identified trends and challenges, focusing on areas with high potential impact.
The process of updating the SRIA will always consider alignment with funding sources and government policies as well as the agenda integration with relevant funding programs, grants, and initiatives.
The Partnership's communication strategy will ensure the information of stakeholders about the updated SRIA, its goals, and the rationale behind the changes through various channels, such as websites, workshops, conferences, and publications. Moreover, a flexible and open feedback mechanism will be established to allows stakeholders to provide ongoing input and insights as the updated SRIA is implemented.

The AWP process will contribute to all three overarching goals and to the impacts of both ERDERA and those set out in the work programme of Horizon Europe. This will be monitored through the ERDERA's monitoring system, captured, and analysed. Specific targets for each objective have been specified in the description of the WP and/or are directly linked and will contribute to the KPIs defined for Operational Objectives. The progress will be reported in the Annual Progress Reports.

Openness, transparency and inclusivity
Openness and transparency have been ensured in ERDERA by promoting the active participation of the entire multistakeholder RD research ecosystem covering the whole pipeline. In terms of geographical coverage, all EU and EEA MS and associated countries were approached during the preparatory phase, to ensure the widest possible geographical involvement. Emphasis has been placed on including countries traditionally underrepresented in RD research. This resulted in 265 institutions from 33 countries expressing their interest in joining the Partnership of which 171 organisations were included. Global international

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collaboration will be further ensured through IRDiRC, and by introducing the expertise of other global actors to specific activities. Patient-centredness and responsiveness to patient-need led research has also been included. Alignment of European and national RD research policies and activities according to the identified needs and priorities of every MS/Associated Country will be ensured through the National Alignment Board (NAB) and National Mirror Groups (NMGs). NMGs will ensure a two-way link with the Partnership, feeding national needs and expertise into the ERDERA's activities, priorities, and outputs and in turn, disseminating the results of the Partnership to the 'grassroots' researcher level. Alignment with the relevant other EU Partnerships, programmes, projects, initiatives (EU-wide and global) will ensure the complementarity and synergies and avoid duplication of efforts. ERDERA will actively engage with complementary fields, such as personalised medicine and digital health. Priorities of ERDERA will be revisited at regular intervals to factor in novel developments in the field and national priorities, involving the whole consortium and the National Alignment Board and will feed the annual planning process. Where possible and required, the advisory governance bodies of ERDERA will be consulted. Dissemination (e.g., workshops and webinars), consultancy and advisory activities will be open to a broader collaborator base and the general public as much as possible. Ultimately, the executive governance layer of the ERDERA will be responsible for an active outreach and liaison with potential partners and identification of cross-cutting activities. Dissemination, awareness-raising and capacity building activities will include a range of measures and tools targeted at different groups and stakeholders. The basis for each Annual Work Programme (AWP) will be the initial multiannual work programme laid out in the Grant Agreement. This will be revised and defined in more detail across the broad annual programming process, which will centre on meetings of the National Alignment Board and Governing Board. As these meetings unite both ERDERA partners and external stakeholders, prioritisation of tasks for finalisation of each AWP will benefit from broad input.

4. Ethics self-assessment

1. Human embryonic stem cells and human embryos		Yes/No	Page
Does this activity involve human embryonic stem cells (hESCs)?		No	
Does this activity involve the use of human embryos?		No	
2. Humans		Yes/No	Page
Does this activity involve human participants?		Yes	From task 6.2 to WP23
If **YES**:	- Are they volunteers for nonmedical studies (e.g. social or human sciences research)?	Yes	From task 20.1, to WP 23
	- Are they healthy volunteers for medical studies?	No	
	- Are they patients for medical studies?	Yes	From task 6.2 to task 12.5
	- Are they potentially vulnerable individuals or groups?	Yes	From task 6.2 to task 12.5
	- Are they children/minors?	Yes	From task 6.2 to task 12.5
	- Are they other persons unable to give informed consent?	Yes	From task 6.2 to task 12.5
Does this activity involve interventions (physical also including imaging technology, behavioural treatments, tracking and tracing, etc) on the study participants?		YES	TASK 8.2-8.3
If **YES**:	- Does it involve invasive techniques?	YES	TASK 8.2-8.3
	- Does it involve collection of biological samples?	YES	TASK 8.2-8.3
Does your activity involve conducting a clinical study as defined by the Clinical Trial Regulation 536/2014 (using pharmaceuticals, biologicals, radiopharmaceuticals, or advanced therapy medicinal products)?		No	
If **YES**:	Is it a clinical trial?	No	
	Is it a low-intervention clinical trial?	No	
3. Human cells / tissues		Yes/No	Page
Does this activity involve the use of human cells or tissues (not covered by section 1)**?**		Yes	WP8
If **YES**:	- Are they human embryonic or foetal cells or tissues?	No	
	- Are they available commercially?	No	
	- Are they obtained within this project?	Yes	WP8
	- Are they obtained from another project, laboratory or institution?	Yes	WP8

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	- Are they obtained from a biobank?		Yes	WP8
4. Personal data			Yes/No	Page
Does this activity involve processing of personal data?			Yes	All WPs
If **YES:**	- Does it involve the processing of special categories of personal data *(e.g. sexual lifestyle, ethnicity, genetic, biometric and health data, political opinion, religious or philosophical beliefs)*?		Yes	From WP6 to WP12
	If **YES**:	- Does it involve processing of genetic, biometric or health data?	Yes	From WP6 to WP12
		- Does it involve profiling, systematic monitoring of individuals, or processing of large-scale of special categories of data or intrusive methods of data processing (such as, surveillance, geolocation, tracking etc.)?	Yes	WP10
Does this activity involve further processing of previously collected personal data (including use of pre-existing data sets or sources, merging existing data sets)?			Yes	From WP6 to task 16.2
Is it planned to export personal data from the EU to non-EU countries?			NO	
If **YES**:	Specify the type of personal data and countries involved			
Is it planned to import personal data from non-EU countries into the EU or from a non-EU country to another non-EU country?			YES	All WPs
If **YES**:	Specify the type of personal data and countries involved: (data on outcome measures and safety after treatment, genomic data and clinical metadata) : Turkey Personal data (name and contact details e.g., email address) of non-EU country researchers will be processed for organisational and dissemination purposes: Serbia, Türkiye, Israel, United Kingdom, Georgia, Morocco, Canada, Australia			All WPs
Does this activity involve the processing of personal data related to criminal convictions or offences?			NO	
5. Animals			Yes/No	Page
Does this activity involve animals?			Yes	WP11 and 21
If **YES**:	Are they vertebrates?		Yes	WP11 and 21
	Are they non-human primates (NHP) (e.g. monkeys, chimpanzees, gorillas, etc.)?		No	
	Are they genetically modified?		No	
	Are they cloned farm animals?		No	
	Are they an endangered species?		No	
6. Non-EU countries			Yes/No	Page
Will some of the activities be carried out in non-EU countries?			YES	FROM WP6 TO WP8
If **YES**:	Specify the countries: TURKEY, U.K			
In case non-EU countries are involved, do the activities undertaken in these countries raise potential ethics issues?			No	

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Is it planned to use local resources (e.g. animal and/or human tissue samples, genetic material, live animals, human remains, materials of historical value, endangered fauna or flora samples, etc.)?		NO	
Is it planned to import any material (other than data) from non-EU countries into the EU or from a non-EU country to another non-EU country? *For data imports, see section 4*		YES	From WP6 to WP8
If **Yes**:	Specify material and countries involved: CSF and serum, Turkey		
Is it planned to export any material (other than data) from the EU to non-EU countries? *For data imports, see section 4*		NO	
Does your activity involve low and/or lower-middle income countries?		No	
Could the situation in the country put the individuals taking part in the activity at risk?		No	
7. Environment, health and safety		Yes/No	Page
Does this activity involve the use of substances or processes that may cause harm to the environment, to animals or plants (during the implementation of the activity or further to the use of the results, as a possible impact)?		NO	
Does this activity deal with endangered fauna and/or flora / protected areas?		NO	
Does this activity involve the use of substances or processes that may cause harm to humans, including those performing the activity (during the implementation of the activity or further to the use of the results, as a possible impact)?		NO	
8. Artificial intelligence		Yes/No	Page
Does this activity involve the development, deployment and/or use of Artificial Intelligence-based systems? *If yes, detail in the self-assessment whether that could raise ethical concerns related to human rights and values and detail how this will be addressed.*		Yes	From WP6 to Task 16.2
Could the AI based system/technique potentially stigmatise or discriminate against people (e.g. based on sex, race, ethnic or social origin, age, genetic features, disability, sexual orientation, language, religion or belief, membership to a political group, or membership to a national minority)?		No	
Does the AI system/technique interact, replace or influence human decision-making processes (e.g. issues affecting human life, health, well-being or human rights, or economic, social or political decisions)?		Yes	
Does the AI system/technique have the potential to lead to negative social (e.g. on democracy, media, labour market, freedoms, educational choices, mass surveillance) and/or environmental impacts either through intended applications or plausible alternative uses?		No	
Does the AI to be developed/used in the project raise any other ethical issues not covered by the questions above?		No	
9. Other ethics issues		Yes/No	Page

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Are there any other ethics issues that should be taken into consideration?	NO	

Ethics self-assessment

Following the completion of the ethics issue table above, below is the ethics self-assessment

Ethical dimension of the objectives, methodology and likely impact

The below explanation addresses the identified issues in relation to:

- *objectives of the activities (e.g. study of vulnerable populations, etc.)*
- *methodology (e.g. clinical trials, involvement of children, protection of personal data, etc.)*
- *the potential impact of the activities (e.g. environmental damage, stigmatisation of particular social groups, political or financial adverse consequences, misuse, etc.)*

ERDERA foresees research activities involving animals and rare disease patients, including children and other vulnerable populations.
Human subjects will be involved in most of the activities planned by ERDERA and in the funded projects. The following aspects has been considered:

- the interventions (blood samples)
- the use of human cells/tissues prospectively and previously collected from patients including children and/or stored in a biobank, and the related processing of (previously collected) personal health data from minors, possibly genetic data, as detailed below.
- the prospective and retrospective processing of health and genetic data from patients, including minors (WP 6 - 12)
- the prospective collection of health data from patients PROs and other health data with surveillance in registries and EHR (WP10)
- the use of mHealth technologies implementing geolocation to collect patient self-reported data (WP10).

Various planned activities deal with the use of personal data including surveys and training activities (within WP 21, and 23) as well as communication and dissemination activities and other with the use or re-use of special categories of data including the health and genetic ones.
Personal data will not be exported from the EU to non-EU countries. On the other hand, health data (i.e. data on outcome measures and safety after treatment, genomic data and clinical metadata) will be imported from project partners from Turkey, into the EU.
In addition, personal data (name and contact details e.g., email address) of non-EU country (Serbia, Türkiye, Israel, United Kingdom, Georgia, Morocco, Canada, Australia) researchers will be imported for organisational and dissemination purposes into the EU.
With regards to animal research studies, the use of vertebrates (mice) is foreseen for preclinical studies in WP11 and WP21.
The project does not plan to use any local resources of non-EU countries, because they will not be involved in the handling of human samples and animal studies.
Results from this project will be of benefit for all countries involved, facilitating the rare diseases research.
Considering the health-research purposes of the project and the proposed strong measures for data protection and for the lawful and ethical conduct of research, as described in the project, neither ethics risks nor misuse of data nor impact of the proposed activities to the rare disease patients safety, well-being and rights are envisaged.
Finally, the project proposal aims to adopt Artificial Intelligence (AI) methods within the Data services Hub. AI models will be used in the studies of different diseases involving patients data. No ethical concerns related to human rights and values are expected.
In fact, AI approaches is proposed to

- support FAIRification. This is restricted to suggesting ontology-based annotations for data elements and values, which are validated by data stewards. The performance of this hybrid

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intelligence will be assessed and compared to that of a purely manual approach to minimize annotation errors and bias.
- for multi-omics and multimodal integrations intended to be explainable, i.e., the results of the methods can be understandable and trusted by human users. To these goals, we mainly work on methods based on networks, such as data integration with knowledge graphs, pathway-level interpretations.

Importantly, these types of approach allow using prior knowledge, and overall permit better technical robustness.
The social acceptance and context will be a part of the design of the DSH requirements in WP13, and the operation environment oriented to the use of the results by health professionals and health researchers.
The application of AI will be reliable and avoiding the potential risks of harming even unintentionally. The methods which will be used (knowledge graphs, pathway-level interpretations, ontology-based methods, or neural networks based methods among others) will be provided with the required level of "explainability" and "interpretability" of the decisions suggested, discarding methods which are not able to provide the sufficient level of explanation with the current available techniques (e.g. SHAP, LIME, etc.).
Importantly, the above ethics-assessment is referred to project research activities. In addition, in the framework of the Funding Work Stream, ERDERA also foresees the funding of research projects, namely Joint Translational Calls (JTCs) that may encompass both non-clinical and clinical research, Clinical Trials (as defined under Regulation (EC) 536/2014) and Networking Support Scheme, that foresees the organisation of networking events. Relevant requirements will be included in the text of respective calls. For each project, the ethics self-assessment will be performed to specifically address the applicable ethics issues, as well as the ethics assessment and follow up, to ensure that the Horizon framework for ethics is fully applied.

Compliance with ethical principles and relevant legislation

Description of how the issue(s) identified in the ethics issues table above will be addressed in order to adhere to the ethical principles and what will be done to ensure that the activities are compliant with the EU/national legal and ethical requirements of the country or countries where the tasks are to be carried out. It is reminded that for activities performed in a non-EU countries, they should also be allowed in at least one EU Member State.

Highest ethical standards will be implemented for the whole duration of the project. To this aim, all partners will comply with the applicable national/local and international ethical provisions. The EU provisions will be applied both in EU and outside.

To guarantee and support ethics compliance of all project activities, a Task will be fully dedicated to ethics (Task 1.5). An internal Ethics Advisory Group (EAG) will be set up and the ethics assessment and/or follow-up of funded projects will be performed. In addition, EAG will update the consortium on the news from the EU framework. Moreover, according to the European Commission provisions, an Independent Ethics Advisor will be appointed. Close collaboration with the Regulatory Support Group (WP18) will be foreseen, as well, to ensure alignment on the ethical and regulatory strategy and to jointly address non-clinical and clinical issues being both ethical and regulatory.

Specifically:

HUMANS will be involved in most of the planned activities. Particular attention will be paid to activities involving vulnerable participants.

The provisions of the Declaration of Helsinki, the Oviedo Bioethics Convention and its Additional Protocol, the CIOMS-WHO International Ethical Guidelines (2016), CoE Recommendations No. R (97) and CM/Rec(2016)6 will be followed. In addition, the 2017 EC Ethical paediatric recommendations will be followed for clinical studies with minors, and Additional Protocol on Genetic Testing for Health

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Purposes (Council of the EU 2008), UNESCO International Declaration on Human Genetic Data, 2003, CoE Rec(92) 3 1992 in case of genetic data processing.

For the primary and secondary use of health data, the necessary ethics approvals will be obtained, informed consent and assent/agreement from minors will be sought. The secondary use of data from European Reference Network (ERN) registries will use the informed consent form template developed in the framework of EJP RD and available in 26 EU languages. In case of processing of genetic data, the development of an incidental findings policy will be implemented.

When handling human cells/tissues, the EU Directive 2004/23 will be followed and compliance with the applicable laws will be guaranteed in all countries involved. The source of cell/tissues will be verified, the necessary authorisations for using or producing them will be obtained. Verification of the informed consent obtained from donors/subjects will be made.

Various planned activities deal with the use of PERSONAL DATA, e.g. surveys and workshops, and others with the use/re-use of health and genetic ones. The processing of such data will be carried out in compliance with Reg (EU) 2016/679, with its related national provisions.

The applied legal basis (including but not limited to informed consent) will be verified before any data processing activity starts.

Appropriate technical and organisational safeguard measures will be adopted to avoid personal data breaches. The implementation of Data Sharing Agreements will regulate the transfer of data among institutions; they will consider if the processor and the controller are based in EU countries and if any specific adequacy decisions between EU and non-EU countries.
Results of the activities will be disseminated only in an aggregate and anonymised way.

The ANIMAL experiments will be conducted in compliance with the 3Rs principles, and the EU Directive 2010/63, COUNCIL DIRECTIVE 86/609/EEC and the COMMISSION RECOMMENDATION (2007/526/EC). Where applicable, Good Laboratory Practices, as included in DIRECTIVE 2004/10/EC will be followed, as well.

In NON-EU COUNTRIES, the highest ethical standards will be guaranteed and the applicable laws followed.

Relevant authorisations/approvals will be in place for the transfer, e.g. in compliance with Directive 2004/23/EC.

ARTIFICIAL INTELLIGENCE methods adopted within the project will consider the ethical and legal implication of their applications to the care of persons, cyber security services designed for protecting users and digital content providers against cyber-attacks, viruses and fraud.

Provisions from the EC Ethics Guidelines for Trustworthy AI (2019) and from the WHO Guidance on the Ethics and Governance of Artificial Intelligence for Health (2021) will be followed. The 7 ALTAI requirements will be verified for each AI system, in order to detect any potential risk; the EC tool (https://altai.insight-centre.org/Home/HowToComplete) will be used. A risk mitigation plan will be developed, if deemed relevant. Only the techniques with all requirements considered fully fulfilled will be used within the project.

Involved humans will be duly informed about the risks and benefits of the systems. Compliance with the provisions from the proposals for European Regulations on Artificial Intelligence (COM/2021/206 final) and on machinery products (COM/2021/202 final) will be followed, once definitively approved.

4.1. The Ethics Screening Report

The following Ethics categories were identified during the Ethics Review of the submitted proposal

- **HEF**- HUMAN EMBRYONIC STEM CELLS AND HUMAN EMBRYOS
- **H**- HUMANS
- **HCT**- HUMAN CELLS / TISSUES
- **POPD**- PERSONAL DATA

- **A-** ANIMALS
- **NEC**- NON-EU COUNTRIES
- **EPQ**- ENVIRONMENT PROTECTION QUESTION
- **AI**- ARTIFICIAL INTELLIGENCE
- **OEI**- OTHER ETHICS ISSUES

The following Ethics requirements were generated:

Number	Ethics Issues Category	Description	Compliance Date (Month)
1	OEI	Ethics Advisor	1
2	OEI	First report by the Ethics Adviser.	12
3	OEI	The second report by the Ethics Adviser.	24
4	OEI	The third report by the Ethics Adviser.	36
5	OEI	The fourth report by the Ethics Adviser.	48
6	OEI	The fifth report by the Ethics Adviser.	60
7	OEI	Sixth report by the Ethics Adviser.	72
8	OEI	Seventh report by the Ethics Adviser.	84
9	NEC, OEI, HEF	Beneficiaries obligations regarding selected research proposals involving the use of human embryonic stem cells (hESC) or human embryos (hE)	NA (ongoing)

Details of the generated Ethics requirements:

No 1	
Ethics issue categories:	HEF; H; HCT; POPD; A; NEC; EPQ; AI; **OEI**.
Before Signature:	No
Max. compliance date: (Months)	1
Description:	**Ethics Advisor_The proposal already provides for the appointment of an independent Ethics Advisor. Periodic reports by the Ethics Advisor must be submitted to the granting authority at each reporting period together with the periodic reports.** The CVs and declarations of absence of conflict of interest for the selected EA(s) must be kept on file and provided to the granting authority upon request. European Commission Guidance for Ethics Advisors/Boards can be found at: https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/roles-andfunctions-of-ethics-advisory-ethics-advisory-boards-in-ec-funded-projects_he_en.pdf
Status:	When an ethics requirement is substantially altered or cancelled you must provide an explanation in the comments box.
Comments:	None

No 2	
Ethics issue categories:	HEF; H; HCT; POPD; A; NEC; EPQ; AI; **OEI**.
Before Signature:	No

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Max. compliance date: (Months)	12
Description:	**First report by the Ethics Adviser.**
Status:	When an ethics requirement is substantially altered or cancelled you must provide an explanation in the comments box.
Comments:	None

No 3	
Ethics issue categories:	HEF; H; HCT; POPD; A; NEC; EPQ; AI; **OEI**.
Before Signature:	No
Max. compliance date: (Months)	24
Description:	**The second report by the Ethics Adviser.**
Status:	When an ethics requirement is substantially altered or cancelled you must provide an explanation in the comments box.
Comments:	None

No 4	
Ethics issue categories:	HEF; H; HCT; POPD; A; NEC; EPQ; AI; **OEI**.
Before Signature:	No
Max. compliance date: (Months)	36
Description:	**The third report by the Ethics Adviser.**
Status:	When an ethics requirement is substantially altered or cancelled you must provide an explanation in the comments box.
Comments:	None

No 5	
Ethics issue categories:	HEF; H; HCT; POPD; A; NEC; EPQ; AI; **OEI**.
Before Signature:	No
Max. compliance date: (Months)	48
Description:	**The fourth report by the Ethics Adviser.**
Status:	When an ethics requirement is substantially altered or cancelled you must provide an explanation in the comments box.
Comments:	None

No 6	
Ethics issue categories:	HEF; H; HCT; POPD; A; NEC; EPQ; AI; **OEI**.
Before Signature:	No
Max. compliance date: (Months)	60
Description:	**The fifth report by the Ethics Adviser.**

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Status:	When an ethics requirement is substantially altered or cancelled you must provide an explanation in the comments box.
Comments:	None

No 7	
Ethics issue categories:	HEF; H; HCT; POPD; A; NEC; EPQ; AI; **OEI**.
Before Signature:	No
Max. compliance date: (Months)	72
Description:	**The sixth report by the Ethics Adviser.**
Status:	When an ethics requirement is substantially altered or cancelled you must provide an explanation in the comments box.
Comments:	None

No 8	
Ethics issue categories:	HEF; H; HCT; POPD; A; NEC; EPQ; AI; **OEI**.
Before Signature:	No
Max. compliance date: (Months)	84
Description:	**The seventh report by the Ethics Adviser.**
Status:	When an ethics requirement is substantially altered or cancelled you must provide an explanation in the comments box.
Comments:	None

No 9	
Ethics issue categories:	**HEF**; H; HCT; POPD; A; **NEC**; EPQ; AI; **OEI**.
Before Signature:	No
Max. compliance date: (Months)	NA (Ongoing)
Description:	**Beneficiaries obligations regarding selected research proposals involving the use of human embryonic stem cells (hESC) or human embryos (hE). Notwithstanding the stipulations under Article 14 annex 5 of the Grant Agreement, the Coordinator must inform the Granting Authority in writing of any research activity within ERDERA (joint transnational calls, clinical research networks, etc.) that may involve the use of hESC or hE. The ERDERA research components must ensure that each of these activities involving the use of hESC/hE successfully passes a scientific evaluation, during which the necessity of using hESC to achieve the scientific objectives is assessed (or the use of hE is described) by independent scientific experts. Following to that, research projects involving hESC/hE may not start without prior ethics review carried out by the Granting Authority and subsequent decision of the Programme Committee.**
Status:	When an ethics requirement is substantially altered or cancelled you must provide an explanation in the comments box.
Comments:	None

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EUROPEAN RARE DISEASES RESEARCH ALLIANCE

Annual Work Plan Year 1

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ANNUAL WORK PROGRAMME

1. Coherence with part B of the proposal

1.1. Annual Work Programme (AWP) objectives

ERDERA's Objectives

As a reminder, the objectives of the Partnership are represented at three levels and organized according to the Partnership Specific Impact Pathways (PSIPs) presented below (Figure 1). The **General Objectives (GOs) correspond to the long-term impacts** to which ERDERA aims to contribute. The **Specific Objectives (SOs)** reflect medium-term timescale and **correspond directly to the expected outcomes** that the Partnership should achieve or contribute to, in line with its mission, and within its lifetime or, at the latest, at 2034 horizon. Finally, the **Operational Objectives (OOs) are considered as means and resources** and are translated through the activities that will be implemented by the Partnership to accomplish the overarching SO and GO levels.

The GOs are defined in line with the Partnership's vision and mission to improve the health and well-being of people affected by rare diseases (RDs), by delivering concrete health benefits through prevention, diagnosis, and treatment development. It was agreed that they should be inspired by and fully aligned with the goals of IRDiRC.

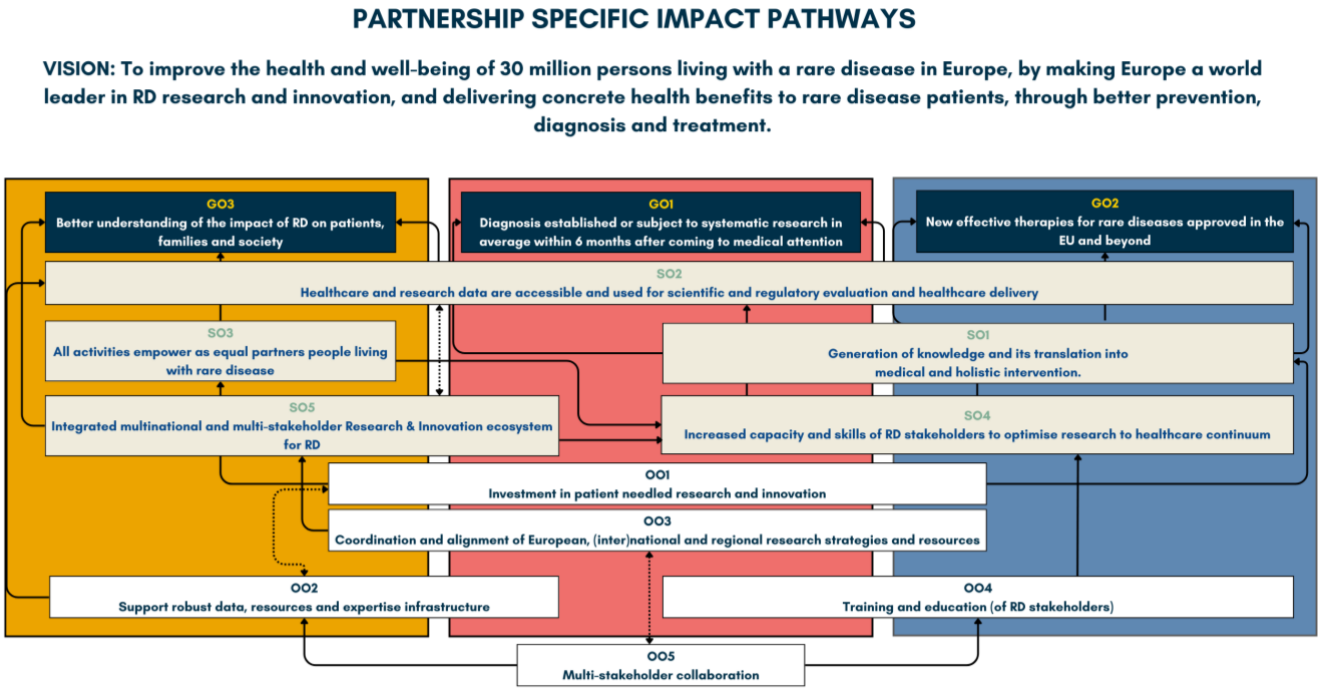


Figure 1. Partnership Specific Pathways of ERDERA (High resolution picture). The interlinks at each level exist: one SO may respond to more than one expected GO. The PSIP represents the most important (strongest) pathways that were agreed during the ERDERA SRIA development after the consultation of SRIA Task Force (more than 80 independent experts) and aggregating more than 500 pathways designed by its individual members. .

GO1: Diagnosis established or enrolment in systematic research in average within 6 months after coming to medical attention (in EU and Associated countries).
Patients with undiagnosed diseases and their families often face an uncertain and unpredictable journey, called a diagnostic odyssey (50% of patients with no final diagnosis, more than 4 years of the diagnostic journey). ERDERA will contribute to shortening the diagnostic pathway for patients with RDs by decreasing time to diagnosis after the first medical appointment with a specialist for those disorders already identified in the literature. For the undiagnosed disorders, efforts will be made to build and/or strengthen the bridge between research and healthcare to provide to every undiagnosed patient the possibility to be included in a globally coordinated diagnostic and research pipeline.
GO2: New effective therapies for rare diseases approved in the EU and beyond.
95% of RDs are still underserved in terms of research and patients with RDs, although diagnosed, face a lack of viable long-term treatment options. To contribute to IRDiRC goals, and more specifically Goal 2 – "1000 new therapies for RDs will be approved, the majority of which will focus on diseases without approved options", ERDERA will accelerate the development of new therapies (especially for diseases without approved options) by providing the necessary expertise and technological support to research projects aimed at developing new effective treatments (encompassing drugs and innovative devices) and by expediting clinical trial readiness of RDs, including contribution to regulatory fitness to enable regulatory approval.

GO3: Better understanding of the impact of RDs on patients, families, and society
Understanding of the impact of RDs on people lives means also better evaluation of the societal and healthcare costs and capacity to implement more inclusive, holistic healthcare approaches. Through required means (funding, data collection, education, awareness raising) and processes (involvement of PLWRD, public engagement) the Partnership will contribute to capturing of RD impact and comprehensive understanding of patients and carers needs leading to more impactful research and, in the long term, improved and/or new processes that will facilitate the diagnosis and care pathways and translate into meaningful societal support.
SO1: Generation of knowledge and its translation into medical intervention.
The Partnership will enable patient-need led relevant science by providing a RD research support pipeline from basic research to clinical trial readiness. Attention will be paid to Social Sciences and Humanities research to better understand the impact of RDs and the potential benefit of new interventions. The integration across value chain will be addressed by combining research financed and performed by both public and private stakeholders and involving patients.
SO2: Healthcare and research data are accessible and used for scientific and regulatory evaluation & healthcare delivery.
ERDERA will support the generation, pooling, integration and sharing of high-quality and interoperable RD data in an expanding ecosystem of distributed FAIR data sources, building on existing infrastructures encompassing ERDRI, the EJP RD Virtual Platform, RD-Connect, and services not specific for RD (e.g., BBMRI-ERIC). It will promote advanced data analysis and data interpretation methods and approaches (both federated and centralised) that exploit this ecosystem. The partnership will also support the development of data-driven computational tools, statistical and AI methods, as well as digital solutions to understand the diseases progression, to solve undiagnosed RD cases and implement new clinical studies/trials designs for small populations.
SO3: All activities empower, as equal partners, people living with rare diseases
The Partnership will provide an inclusive pathway and adequate resources to empower PLWRD and/or representatives as equal partners. PLWRD will be involved at all levels of governance and execution of ERDERA, with training or induction as necessary. A structured, flexible, and coherent framework for patient engagement in research (including funding) will be developed which will be adaptable at national levels and will promote best practices, re-using, and extending existing resources. To reduce inequities between different types of RD, underserved RDs will be targeted through, among others, building new or expanded networks and supporting dedicated research.
SO4: Increased capacity and skills of RD stakeholders to optimize research to healthcare continuum
ERDERA will incorporate capacity building activities as integral part of the RD research pipeline to enable upgrading of scientific, technology, but also regulatory knowledge of stakeholders participating in research projects financed through competitive calls but also those performing "in house" research activities as part of the Clinical Research Network (CRN). Moreover, new generations of RD researchers will be equipped with state-of-the-art competencies. To unlock the access to RD top-level education to all, the Partnership will develop an accredited, comprehensive online education programme taking stock of highly performing pre-existing modules complemented by novel training units.
SO5: Integrated multinational & multi-stakeholder R&I ecosystem for rare diseases.
The Partnership will break the silos between communities by consolidating the already existing strong community and stepping-up the integration of underrepresented perspectives, namely the industry, regulatory bodies, and payers. Through dedicated onboarding mechanisms, ERDERA will gradually bring in additional players to attract and increase the critical mass of resources, know how, talents, and excellence, but also to erase white spots on the RD research map and offer equal opportunities to patients across Europe and beyond. It will catalyse the transfer of good practices to the national and regional level by building or consolidating the RD National Mirror Groups (NMGs). This will be reflected by relevant governance and advisory structures but also overall Partnership organisation to ensure coherence and maximise impact of all actions.

The OOs supporting SOs and GOs and to be reached via activities described here in Section 2 are: **OO1: Investment in patient need-led research and innovation, OO2: Support robust data, resources, and expertise infrastructure, OO3: Coordination and alignment of European, (inter)national and regional research strategies and resources, OO4: Training and education (of RD stakeholders) and OO5: Multi-stakeholder collaboration.**

The following figures reflect on how ERDERA's Work Streams (WS) and their specific work packages (WPs) contribute to the **General (GOs), Specific (SOs) and Operational Objectives (OOs)** set for the programme. Figure

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2 demonstrates the % of activities/tasks that aligns with respective GO and the overall commitment share among the three GOs. Figure 3 specifies how each WP contributes to the SOs by aligning individual tasks with these objectives. Finally, the Figure 4 and Figure 5 show how OOs, and therefore specific resources, are employed within each WP and interaction trends between WPs and the GOs, SOs, and OO, respectively.

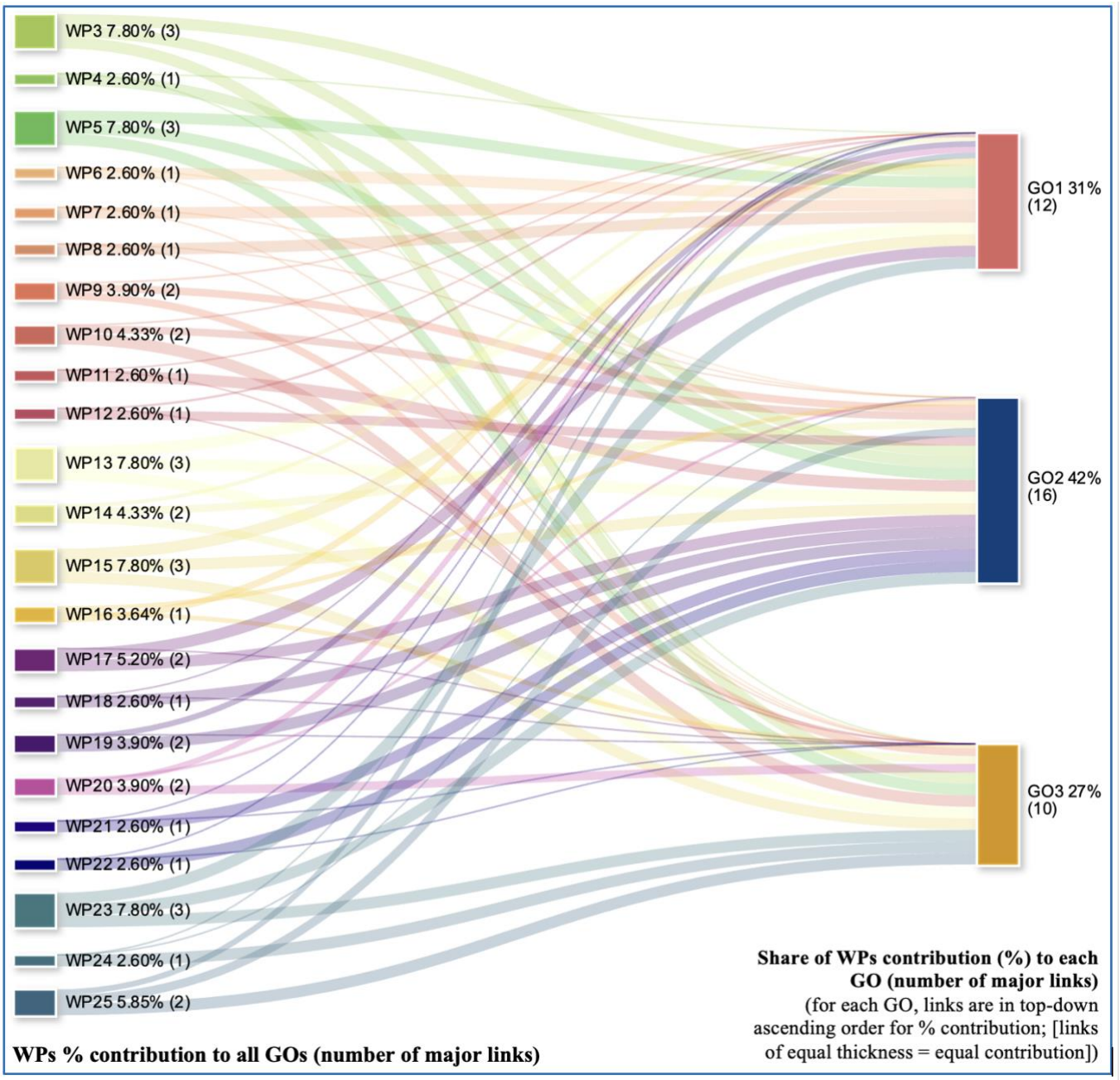


Figure 2. Work Package relative contribution to the General Objectives based on the number of tasks involved.

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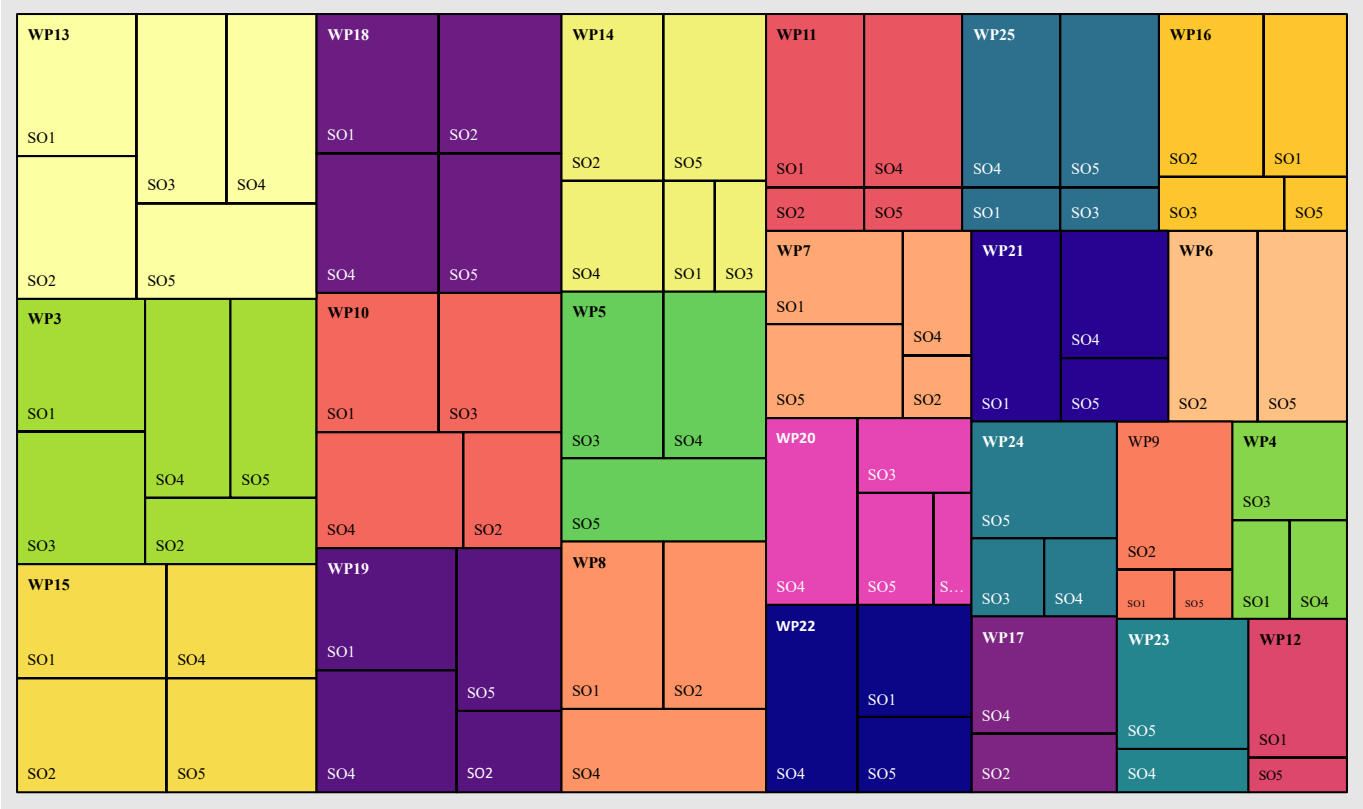


Figure 3. Work Package relative contribution to the Specific Objectives based on the number of tasks involved
(highest=upper left corner, descending=first down, then right, lowest=bottom right corner).

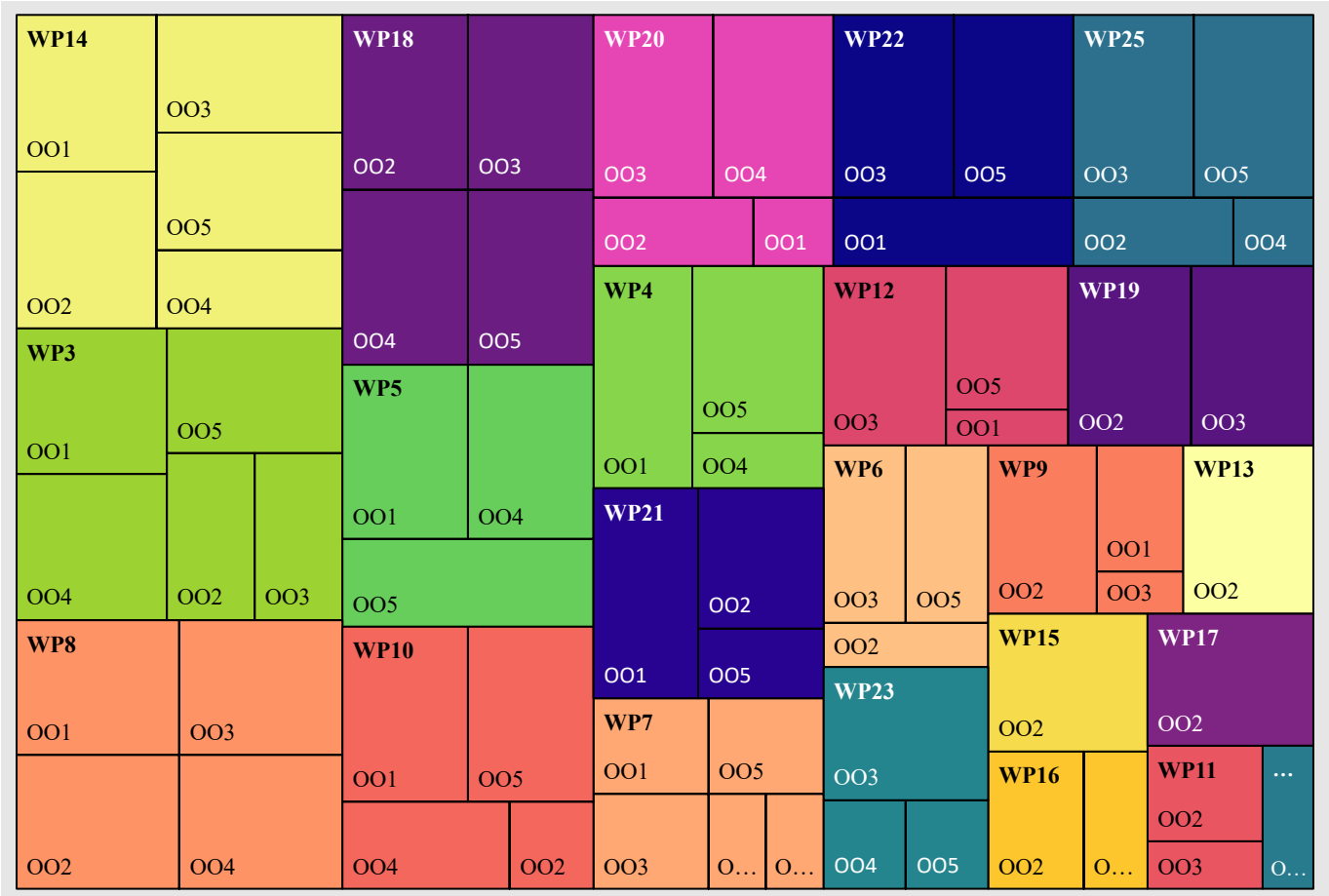


Figure 4. Work Package relative contribution to the Operational Objectives based on the number of tasks involved
(highest=upper left corner, descending=first down, then right, lowest=bottom right corner).

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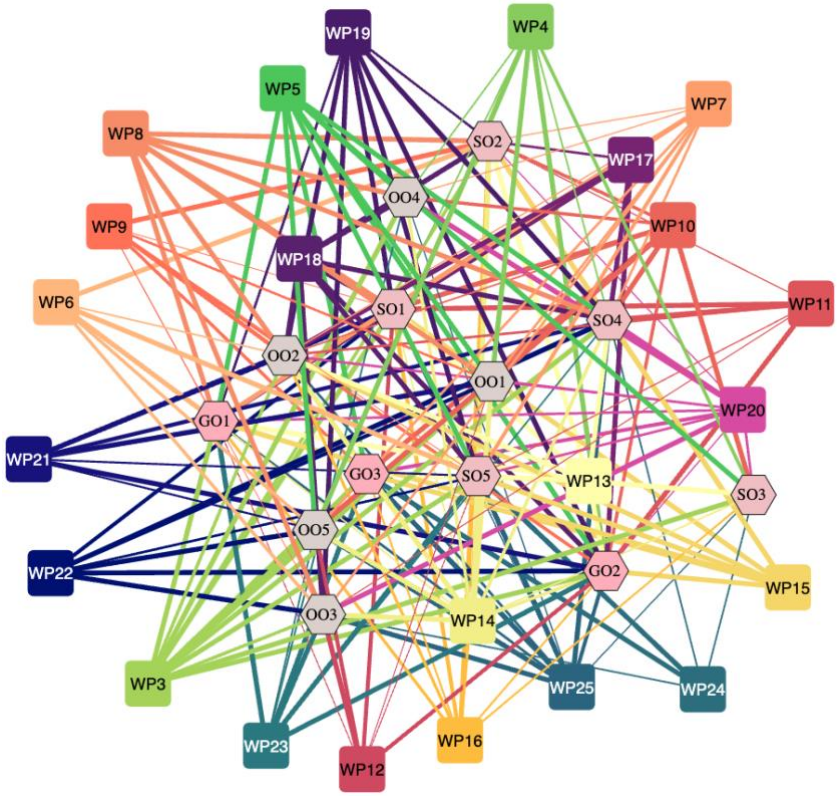


Figure 5. Work Package links to Operational, Specific and General Objectives. The more connections, the larger the node. The interaction line thickness represents the contribution relative score based on the number of tasks in each work package contributing to an objective.

It is thus expected that the objectives defined for the Year 1 of the Partnership will align with these overarching contributions. This will be monitored through the ERDERA's monitoring system, captured, and analysed. Specific targets for each objective have been specified in the description of the WP and/or are directly linked and will contribute to the KPIs defined for Operational Objectives. The progress will be reported in the Annual Progress Report.

The Year 1 objectives of ERDERA are organized within each ERDERA's block/WSs as follows:

Coordination & strategy
Objective 1: Establish day-to-day management office to ensure efficient financial administration (budgeting, planning, accounting), Grant Agreement-bound reporting, data management plan and risk overseeing and mitigation tactic. *Objective 2:* Develop & provide tools for assisting efficient and impactful governance and strategy, including decision-making processes, supervision of Patient & Public Engagement and Involvement (PPIE) and functioning of respective governing bodies (Governing Boards, Executive Committee, and Multistakeholder Advisory Board (MAB), etc.). *Objective 3:* Build (based on the already well-established EJP RD system) internal management and monitoring systems to allow smooth interaction of all project partners, regular internal communication, and assessment of progress and challenges necessary to feed the decision-making process, strategy, and sustainability. *Objective 4:* Guarantee the implementation and compliance with relevant ethical standards in all activities. *Objective 5:* Develop ERDERA's brand and raise awareness about its vision and mission, continuing the process of its positioning as a pivotal actor to advance RD research and build the RD ecosystem in Europe and beyond.

Objective 6: Design the communication and dissemination (C&D) strategy that supports long-term ERDERA's objectives and all WPs in their communication needs, facilitating the necessary tools and materials and ensure consistency and alignment with the overall communication strategy and plans.

Objective 7: In collaboration with all WS and partners', comms representatives promote available resources, activities, and calls, communicate progress made and disseminate results to build ERDERA's reputation as an enabler of innovative, standardised, streamlined, and collaborative transnational RD research.

Funding Work Stream

Objective 8: Implement first joint transnational call.

Objective 9: Develop the framework of the clinical trial call.

Objective 10: Set up and launch the Networking Support Scheme.

Clinical Research Network

Objective 11: Instigate the establishment of the CRN diagnostic data availability and collation effort that comprises ERNs, national UDPs and national diagnostic centres so that 10,000 data sets can be shared during the first 12 months.

Objective 12: Instigate the implementation of data standardisation, sharing, federation and quality control so that data analysis methodologies can be applied.

Objective 13: Set up the processes to enable access and federation of data for re-analysis of large datasets and return research results to the clinics, to RD patients and their families.

Objective 14: Start the re-analysis of existing data following a distributed approach while starting preparations for a federated model to discover novel diagnoses.

Objective 15: Kick-start the organisation of variant interpretation and the development of best practices to improve this activity across disease groups and ERNs.

Objective 16: Enable access of complete genome sequencing for RDs in underrepresented countries.

Objective 17: Make multiple RWD data sets available for data integration and optimise the data quality of available data sets.

Objective 18: Establish the legal and formal prerequisites for extraction of primary healthcare data.

Objective 19: Establish the overall regulatory strategy for development and validation of PCOMs in RDs.

Objective 20: Develop the study protocols for targeted use cases including selection of PROMs, and end-user requirements both clinical and technological.

Objective 21: Identify the most urgent and suitable disease groups for ATMP therapies.

Objective 22: Start working on all aspects of the N-of-few platforms including consensus on patient identification criteria and first outcome measures, trial design, and treatment site criteria for N-of-1 treatments.

Data Services Hub

Objective 23: To organise the workflow and to technically lead the teams of Data Services Hub + CRN/JTC/CT researchers and developers to ensure a perfect alignment of Data Services Hub activities from Year 1 onwards. Ultimately to effectively complete projects that result in increasing numbers of stakeholders contributing to the Data Hub as value proposition (effectuate the CTO role).

Objective 24: Scale up the federated infrastructure built in EJP RD (RD-VP) by evolving a service-oriented architecture (SOA) to accommodate data, knowledge, and analysis methods from related CRN/JTC/CT projects.

Objective 25: Onboard sets of resources, to make them automatically findable within the SOA-based ecosystem, accessible under well-defined conditions, interoperable based on the ecosystem's implementation guidelines, and reusable (allow for querying and reusing data within the connected resources).

Objective 26: Provide the requirements and design the workflow to efficiently organise interdisciplinary data readiness teams executing FAIR data creation and FAIR data processing.

Objective 27: Provide a first prototype of design of project ingestion tooling.

Objective 28: Study the data kinds and quality (RWD, Synthetic, clinical trial collected, etc.) required in at least 2 pilot cases coming from WP9 and improve the interoperability of platforms for this purpose.

Objective 29: Provide tools and services for RD partners to prepare data for the regulatory pathway in drug development, in collaboration with WP18, including clinical collected data and synthetic data.

Objective 30: Start the contribution to the design and use of a Data Hub personal data control that guarantees that individuals can have access to data records derived from them and, to set data record use conditions.

Objective 31: First release of analysis ready reference deployments of the ERDERA analysis infrastructure, including support and interoperability with WP13-15 data ingestion, and ability to scale to cloud computing matching CRN prioritised needs.

Objective 32: Collect and develop protocols, software, and pipelines for large data sets and high-performance computing (HPC) analyses and deploy to the infrastructure, with priority on CRN first analysis objectives.

Objective 33: Collect and develop protocols, software, and systems that enable federated data analysis use cases and pilots, with focus on a demonstrator that integrates the main federated analysis frameworks.

Objective 34: Define first research question for RD Maps towards years-3 proof-of-concept.

Objective 35: Start specifying the requirements for use of the specified knowledge bases and their assess interoperability needs to connect them to RD Maps.

Expertise Services Hub

Objective 36: Continue and further expand the successful EJP RD mentoring program accompanying funded projects starting at the design phase and if required also during project development.

Objective 37: Initiating a feasibility study of a potential workflow for additional expert support based on a consultancy service-based model.

Objective 38: Create a one-stop point for regulatory scientific questions related to preclinical and clinical research in the form of a dedicated project Regulatory Support Group.

Objective 39: Start developing new regulatory support tools to facilitate more effective translation of new therapies to the clinic.

Objective 40: Start operational activities to provide advice on opportunities, strategy, and timings to engage with regulatory agencies, including the qualification of novel methodologies and standards to streamline new therapeutic development for RD at the appropriate time.

Objective 41: Provide the necessary guidance required to support efficient, regulatory-compliant first in man clinical trials.

Objective 42: Initiate the methodological knowledge transfer, whereby at least one concrete (clinical) case will be identified.

Objective 43: Identify and review methods available for the use of Real-World Data (RWD), RDs design and analysis, when data are hierarchical, incomplete, and/or of different data types as well as of a non-parametric, pharmacometrics, and randomization-based nature.

Education & Training

Objective 44: Empower first cohorts of patient representatives (including paediatric patients) to enable their full-scale involvement into RD research for patient-centricity.

Objective 45: Support the RD-focused career development of young researchers through mutual learning with patient representatives.

Objective 46: Build the foundations of a European University Diploma on RD research.

Objective 47: Develop a first set of online and face-to-face trainings for the RD community following 5 main training tracks: diagnostic research, clinical research, research methodologies, clinical trials and management, and data research.

Objective 48: Support wide dissemination of education and training to be developed in Year 1 into national systems through the train-the-trainer principle.

Acceleration Hub

For the ATMP Technology Accelerator:

Objective 49: Define starting materials (plasmids, cell line, etc.) that can adequately support rAAV manufacture.

Objective 50: Optimize RNA sequence design to provide higher stability, long-lasting efficacy, and tissue/cell-specific expression.

Objective 51: Investigate mechanisms underlying extracellular interactions and intracellular processing of LNPs/EVs to better understand LNPs/EVs uptake and trafficking, endosomal escape, delivery, macromolecular interactions, and biophysical processes in the cytosol of host cells and associated innate immune/inflammatory responses.
Objective 52: In vitro selection of editing tools (i.e., combination of editing enzymes and gRNAs) and bespoke gene editing reagents to correct disease-causing mutations affecting human Hematopoietic Stem and Progenitor Cells (HSPCs), the central nervous system and the retina, and the liver and the muscle.

Objective 53: Define test formats of different platforms used by the various partners of WP21 for in depth-assessment of immune reactivity and outline of a test strategy to get best comparability between labs.

For the PPP Accelerator:
Objective 54: Create workflows and legal documentation necessary to structurally identify, evaluate and select projects, the liaison with third party investors and innovation funders and the definition and readiness of the project selection process for the PPP Accelerator.

Inter(national) Alignment

Objective 55: Develop or consolidate at least 23 NMGs including definition of their mandate, constitution of the National Alignment Board and organization of the first NMG annual meeting.

Objective 56: Map the strategic alliances with initiatives outside ERDERA and prepare the enrolment of possible collaborations by developing formal documentation (MoU models).

Objective 57: Support IRDiRC consortium (its 7 committees) and its planned activities (Task Forces) through the Scientific Secretariat office.

Objective 58: Contribute to the internationalisation of the CRN by preparing the 2nd International CRN Conference based on the outputs gathered from the first conference edition, and in collaboration with the ERDERA's CRN stakeholders and their USA equivalents.

Objective 59: Build the governance of the ERN Living Lab, identify relevant stakeholders, and support dissemination of ERDERA's activities to ERN members.

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Objective 60: Map capabilities, assets, and capacity development of underrepresented countries.

Objective 61: Build synergies with the network of national contact points for health and widening aspects of Horizon Europe.

Objective 62: Define preliminary measures to boost inclusion of UCs in ERDERA funded projects.

1.2. Expected impacts

The AWP of Year 1 will contribute to all three overarching goals and impacts of ERDERA and impact set out in the work programme of Horizon Europe (see also Part B of the proposal, section Impact). The concrete contributions will be measured through linked Key Performance Indicators (KPIs). The table below specifies the indicators that will be captured within the first year. ERDERA's monitoring system will enable collection of data necessary to measure the progress towards, and achievement of objectives and impact of the AWP Year 1.

European Partnership [European Rare Diseases Research Alliance]				**Monitoring and evaluation framework**	
Overall vision: To improve the health and well-being of 30 million persons living with a rare disease in Europe, **by making Europe a world leader in RD research and innovation**, and delivering concrete health benefits to rare disease patients, through better prevention, diagnosis, and treatment.					
Objectives		**What is a measure of success?**	**Which is the data source | and methodology used** [project data, study, ….] **| Unit of measurement**	**Who is responsible for monitoring and providing the data/ information When will it be collected?**	**Baseline and target**
Specific objectives* (linked to outcome/result indicators)	SO2	Use of data sources	ERDERA Data Hub & monitoring system | increase of access to research data sources through the Virtual Platform | %	Responsible: Data services Hub Work Packages leaders. Assessment frequency: Yearly.	**Baseline:** Number of VP Access at the end of EJP RD. **Target: Y0:** +5% **Y1:** +5%.
	SO3	Capacity building of RD patients	Training activity surveys & monitoring system | Number of patients empowered, within the Partnership, through capacity-building and training activities related to research | Number patients participated at training activities per year	**Responsible:** Workstream Education and Training leaders & PPIE. **Assessment frequency:** Yearly.	**Baseline:** Historic data from EJP RD : 350 per year. **Target:** Y1: 2500-3000 every year
	SO3	Patients involved in RD funded projects	Funding workstream reports; Project reports; & monitoring system | Percentage of funded research projects that involve patient organisations as co-designers. | Percentage	**Responsible:** RD funding Workstreams leaders & PPIE. **Assessment frequency:** Yearly.	Baseline: Historic data from EJP RD: 60%. **Target: Y1:** 70%.
Operational objectives* (linked to output indicators)	OO2	Integrated Data Service infrastructure	ERDERA Data-Hub, monitoring system & coordination and Management workflow | Services provided by the integrated data infrastructure | Number	**Responsible:** Data Services Hubs WP and task leaders, and Coordination team. Assessment frequency: yearly.	**Baseline:** 0. **Target: Y1:** 30.
	OO2	Integrated Expertise Services infrastructure	ERDERA Data-Hub, monitoring system & coordination and Management workflow | Services provided (i.e., ELSI, IPR, regulatory, methodology, etc.) by the integrated expertise infrastructure | Number	**Responsible:** Expertise & Data Services Hubs WP & Task leaders, and Coordination team. Assessment frequency: yearly.	**Baseline:** 0. **Target: Y1:** 20.
	OO3	NMGs created/ functioning	International Capacity Alignment workstream (WPs) reports & ERDERA	**Responsible:** International Capacity	**Baseline:** 4. **Target: Y1:** 14.

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			monitoring system | Total number of NMG operational | Number	Alignment WP and Task Leaders. **Assessment frequency:** Y1 and Y2.	
	OO3	Interactions/projects with non-EU entities	International Capacity Alignment workstream (WPs) reports & ERDERA monitoring system | Total number of interactions (e.g., good practices, harmonisation)/projects with International legal entities | Number	**Responsible:** International Capacity Alignment WP and Task Leaders. **Assessment frequency:** yearly.	**Baseline:** 0. **Target: Y1:** 1.
	OO4	Capacity building	Data & Reports from Workstreams Education and Training & ERDERA monitoring system | Number of researchers/stakeholders having benefited from upskilling activities (through training, mobility, and access to infrastructures) | Number	**Responsible:** ERDERA monitoring task leaders in coordination with training leaders & contributors. **Assessment frequency:** yearly.	**Baseline:** Historic data from EJP RD : 2500-3000 per year. **Target: Y1:** 4640.
	OO4	Funding invested into capacity building activities	ERDERA monitoring system & coordination and Management workflow, ERDERA periodic reports | Total Funding committed for training, mobility, and access to infrastructures | Million €	Responsible: ERDERA Coordination team & ERDERA monitoring task leaders. Assessment frequency: yearly.	**Baseline:** Historic data from EJP RD : 6.5M€ (overall budget for Training & education activities). **Target:** Y1: commitment every year of 1.2M.
	OO5	Expansion to new stakeholders	ERDERA monitoring system & coordination and Management workflow | Number of new stakeholder (by category) involved with ERDERA after launch | Number by category of stakeholders	**Responsible:** ERDERA Coordination team & ERDERA monitoring task leaders. **Assessment frequency:** yearly	**Baseline:** 94 beneficiaries in EJP RD, and 152 beneficiaries + 19 associated partners in ERDERA. **Target: Y1:** +10.

1.3. Correspondence with part B of the proposal

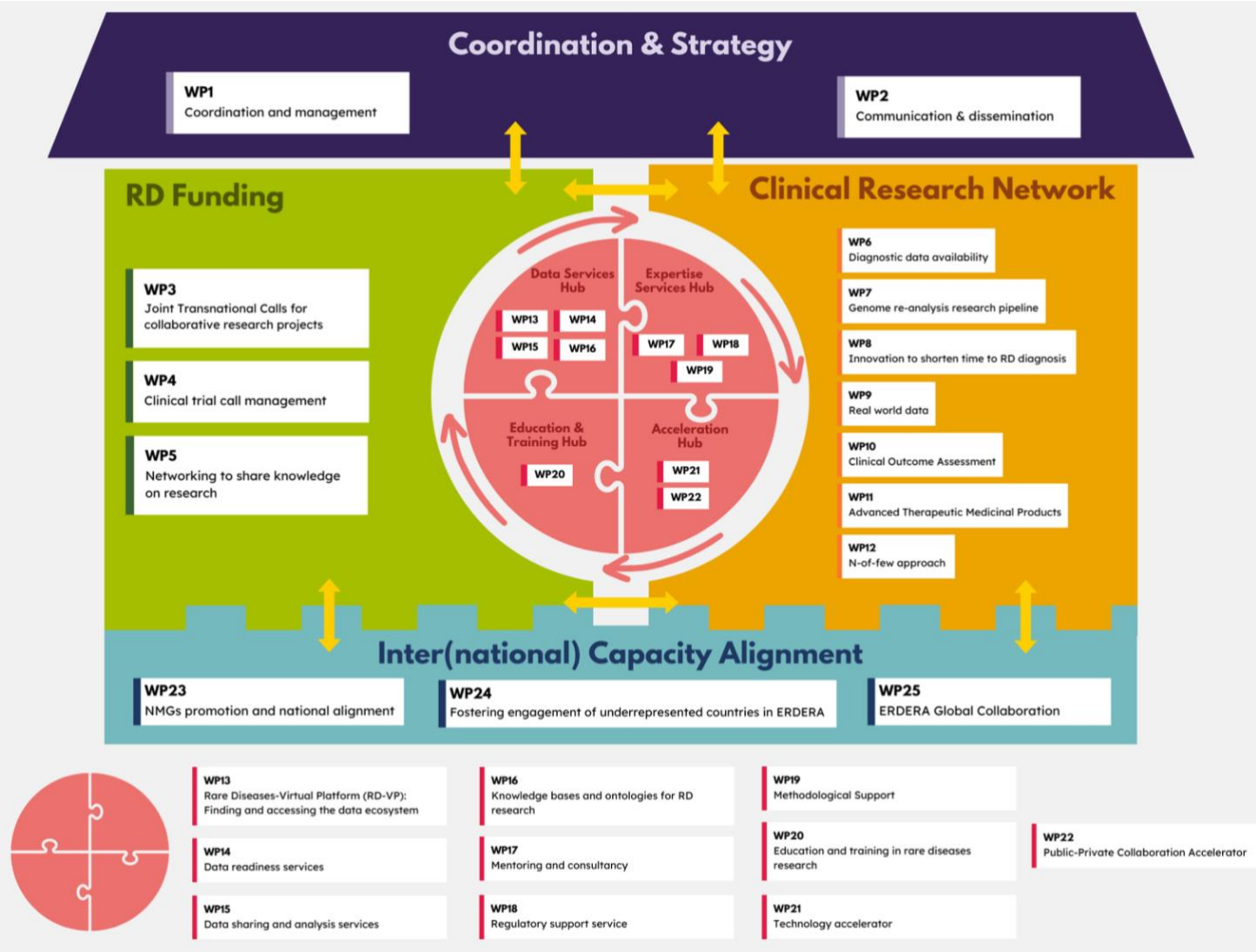
The 1st AWP of ERDERA is fully aligned with the scope and challenges of the Partnership as presented in part B. To that end, the AWP recalls the State of the Art and Methodology underpinning each WP and precises how the activities of Year 1 fit in the overall strategy and actions of each WP.

2. Annual Work Programme Activities

2.1. Annual Work Programme

2.1.1. Structure of the Annual Work Programme

The Annual Work Plan is organised in 25 Work Packages fully aligned with the Description of Action (Part B of the proposal).
The following figure shows the overall structure of ERDERA:



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2.1.2.Timing of the different programmed activities and their components

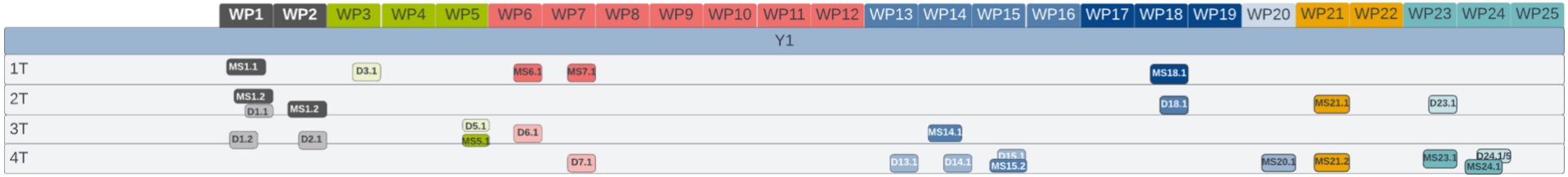


Figure 1. Collapsed view of Year1 Deliverables and Milestones (**high resolution picture**)

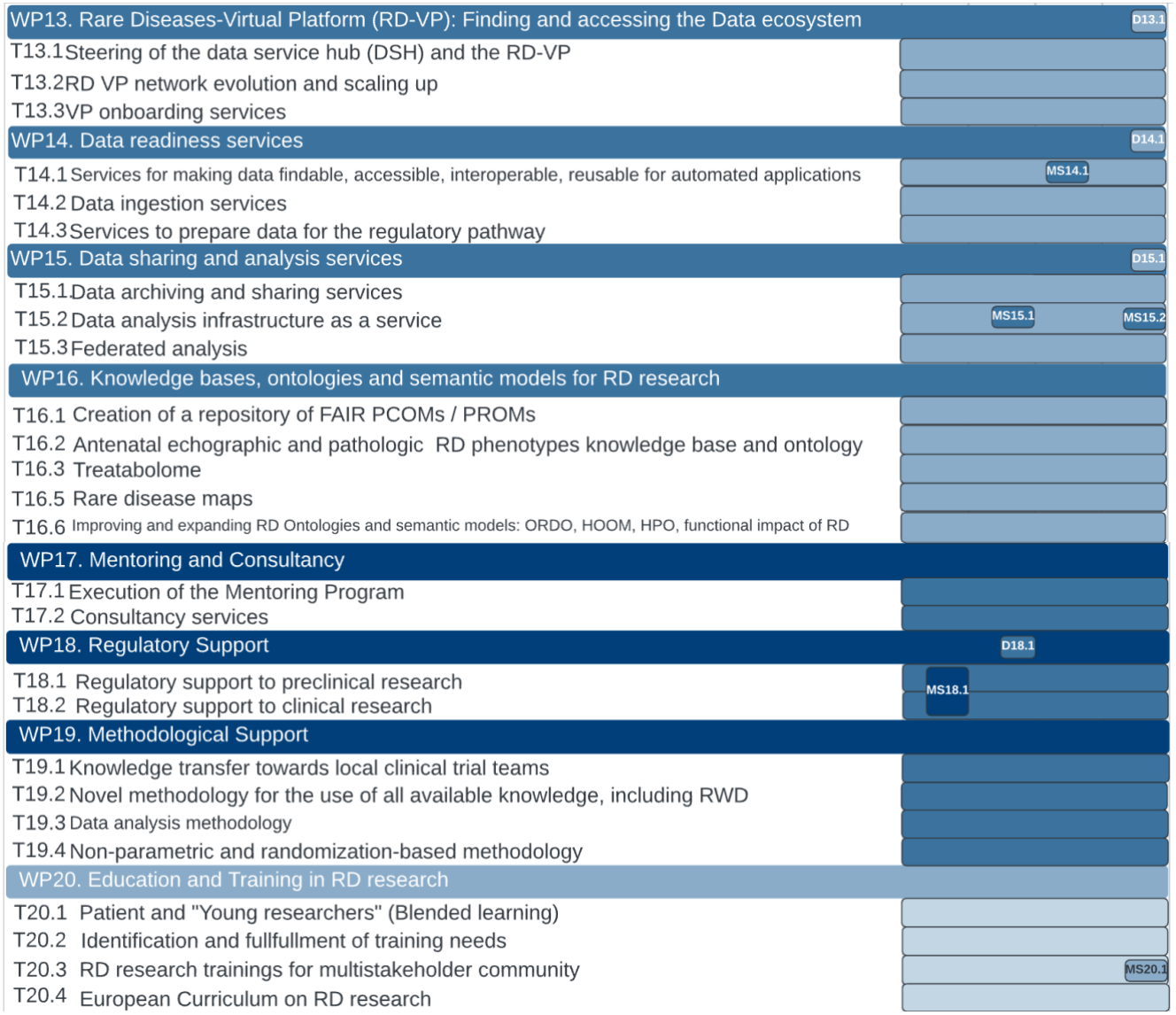
Below, the Gantt for the Year one:



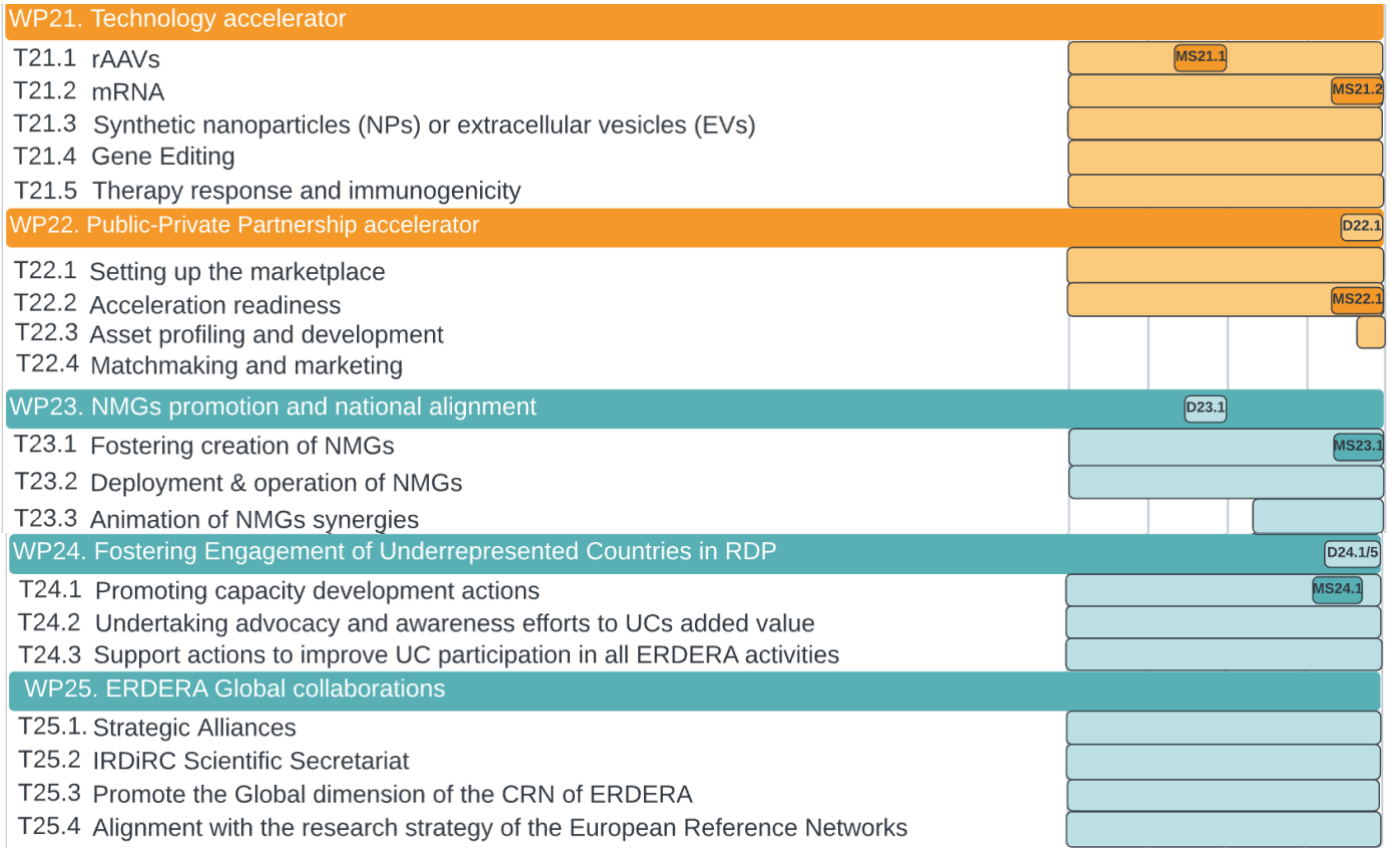
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2.1.3. Detailed work description

2.1.3.1. Description of each set of programmed activities and the relevant work package

Table 2.3.a: Annual Work Programme Activities for each set of activities:
The description of each work package encompasses state-of-the-art and methodology sections.
The indicated participating organisations encompasses partners for which specific person-months were allocated as well as other contributors (Beneficiaries and Associated Partners participating in-kind and thus with no indication of person-months)

Set of Activities Number	**1**	**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Coordination & Management**					
Short name of participant & (No)	INSERM_IT-GGB (1)	CVBF (50)	FGB (23)	TEAMIT (2)	EURORDIS (26)	HRCI (135)	RDI (34)
Person Months	90	6	12	12	4	1.8	1.8
Short name of participant & (No)	AFM (30)	GA UK *(168)	WDO (120)	CSO-MOH (49)	CE (47)	TEKKARE (106)	MSW (137)
Person Months	2.8	1.8	1.8	6	18	28	15
Short name of participant & (No)	ANR (4)	DLR (3)	ZonMw (7)	AICIB (32)	AUMC (20)	VULSK (27)	DDF (51)**
Person Months	1	1	1	1	1	1	
Start month	M1		**End month**	M12			
**Associated partners providing in-kind contribution*							
*** Beneficiaries providing in-kind contribution*							
State of the art behind this WP							
The state of the art behind the coordination and the management of the ERDERA project is deeply rooted in the successful precedent set by the European Joint Program on Rare Diseases (EJP RD), also coordinated by INSERM_IT-GGB. Indeed, EJP RD constituted at its launch a major milestone as a prime example of Member States working together in a coordinated manner and on a more integrative and cross sectorial approach to tackle health challenges related to rare diseases. From this perspective and following the EJP RD, the ambition of the ERDERA project is to build on the successes of the EJP RD and provide solutions to address the key R&I bottlenecks identified that hinder the effective development of better diagnostics, therapies and research-enabled care in the field of R&D. Building upon the invaluable experience gained during the EJP RD project by the INSERM coordination team, the ERDERA project aims to seamlessly continue and expand upon the effective coordination and management practices. The EJP RD served as a pivotal learning experience, offering invaluable insights into orchestrating large-scale, international research collaborations focused on rare diseases. The ERDERA project is committed to not only preserving but also enhancing the effective coordination and management practices that were instrumental in the success of the EJP RD project. This evolution is vital given the ever-evolving landscape of rare disease research, the increasing complexity of international research initiatives and the ambitious of the ERDERA, going further than							

EJP RD.
INSERM, the ERDERA coordination institution, with its proven track record during the EJP RD development and lifetime, will once again take the lead in guiding ERDERA towards its objectives. With its rich history of efficiently managing diverse research efforts and fostering seamless collaboration among multidisciplinary teams, INSERM brings a proven track record that instils confidence in the ERDERA consortium. The experience, expertise, and dedication of INSERM will serve as the cornerstone for ERDERA's coordination and management strategy, ensuring that the project continues to meet and exceed its ambitious objectives in the field of rare disease research.

Methodology

The methodology approach in the Coordination and Management WP of the ERDERA is characterized by a comprehensive framework that has evolved based on the EJP RD project's experiences and best practices. It places a strong emphasis on meticulous project planning, resource allocation, and the establishment of highly efficient communication channels. Project planning involves the development of clear objectives, milestones, and timelines, ensuring that each aspect of the ERDERA partnership aligns with its overarching goals. Resource allocation is executed with precision, considering the diverse needs of the research teams, from funding and equipment to expertise and personnel. This meticulous allocation strategy optimizes the utilization of resources and promotes synergy among consortium members.

Building on the lessons learned from EJP RD, INSERM coordination team has surrounded itself with organisations that are experts in their fields to handle the cross-functional and strategic activities that make up this WP “Coordination and management”.

Objectives

The main objective of this WP is to provide the necessary support for efficient management and coordination of the EU Institute for Rare Diseases. **More specifically, in Year 1 of the ERDERA, WP1 will:**

- Ensure appropriate day-to-day management including financial administration (budgeting, planning, accounting), Grant Agreement-bound reporting, data management plan and risk overseeing and mitigation tactic.
- Develop & provide tools for assisting efficient and impactful governance and strategy, including decision-making processes, supervision of Patient & Public Engagement and Involvement (PPIE) and functioning of respective governing bodies (Governing Boards, Executive Committee, and MAB, etc.).
- Build (based on the already well-established EJP RD system) internal management and monitoring systems to allow smooth interaction of all project partners, regular internal communication, and assessment of progress and challenges necessary to feed the decision-making process, strategy, and sustainability.
- Start the development of an integrated short and long-term sustainability.
- Guarantee the implementation and compliance with relevant ethical standards in all activities.

Description of Programmed Activities

T1.1. Day-to-Day management and coordination (M1-M12) *TL: INSERM_IT-GGB; Contributors: TEAMIT.* T1.1. aligns with GO1-3; SO5; OO3,5.
The coordinator and the Coordination team will be based at INSERM_IT-GGB. The Coordination Team will consist of the coordinator, several project managers, financial officer, and assistant. INSERM_IT-GGB, being responsible for scientific, strategic, and financial coordination will be assisted by TEAMIT to further support contractual obligations, notably the development of annual plans and reports. Such organization of the coordination office is based on the already bulletproof management office of the EJP RD where, under the responsibility of the coordinator, highly qualified project managers directly accompany partners in specific workstream/activities and closely collaborate

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with administrative and financial as well as communication officers to ensure smooth project running and timely problem-solving.

In more detail, the coordination team will provide during Year 1 of the Partnership, support and the overall management structure in: (1) Liaising with the EC; (2) Supporting The decision-making and linkage of project components; (3) Monitoring of the activities and timely preparation and submission of Deliverables and completion of Milestones; (4) Coordinating of the preparation and submission of the periodic Annual Progress Reports, AWP, technical and financial reports and Final Report; (5) Overseeing risk evaluation and mitigation; (6) Daily project functioning and internal communication by setting up specific tools including MS Teams infrastructure, with a library for document management and sharing, events calendar, internal bulletin, etc. as well as of the relevant monitoring system.

ST1.1.1. Coordination & support with and across WPs *STL: INSERM_IT-GGB; Contributors: TEAMIT*
In addition to the continuous assistance to the project partners by the coordination team and to efficiently manage the support and swift communication within and across WPs, the Partnership will rely on two main bodies: the Operating Group (OG) [composed of the WS Leaders, together with the Coordination team], and the Executive Committee (ExCom), [composed of the Coordination team and all WP Leaders].

The OG will meet through regular conference calls (every 3 weeks), staring from M1, to discuss topics of (operational) relevance and ensure adequate reactivity in case of urgent situations and risk management. As such, the OG will be the place for regular update on the activities in all WP to ensure alignment as well as reporting any bottlenecks to the Coordination. Furthermore, the OG will contribute to the preparation of the ExCom meetings.

The ExCom will meet remotely every 3 months and, whenever relevant, jointly with the MAB (or other Advisory and/or Governance body) to report on the advancement of the activities, discuss the priorities and work on the development of the AWP. ExCom will be the forum to discuss details of the Partnership progress and to initiate the discussion on priorities and development of the AWP, including resource utilisation. The first (kick off) meeting of the ExCom is foreseen in M1 of the project.

ST1.1.2. **Ensuring contractual obligations** *STL: TEAMIT; Contributors: INSERM_IT-GGB*
The work will focus on the planning and reporting related to the contractual obligations included in the Grant Agreement. The development of the Annual Progress Report and AWP will follow a structured process managed by the ExCom, in agreement with the General Assembly and submitted to the vote of the Governing Board (GB). ST 1.1.2. Leader will be responsible for setting up reporting mechanisms, supporting, and training Beneficiaries on reporting procedures as needed and coordinating the production of reports. The annual progress reports will be drafted by each WP leader and compiled by the respective WS leaders. TEAMIT will be responsible for the collation of the single progress reports to be complemented by the outcomes of the monitoring and progress against established KPIs.

For the development of the AWP, the ExCom will be asked to propose tasks and deliverables aligned with: (i) Recommendations provided by the MAB and GB based on their judgement of the Partnership progress as well as strategic priorities included in the SRIA; (ii) Internal consultation for each WP and in line with their implementation status and the overall Partnership planning (initial proposal).

This will include an update of the budgetary plan and the proposal for the redistribution of funds and, if needed, new responsibilities. The full AWP draft will be presented to the General Assembly and open for its comments before having its final presentation at the face-to-face meeting with MAB and GB. The finalized version of AWP will be validated by the GB before sending to the Commission.

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In the Year 1 of the ERDERA, it is planned to deliver the AWP for the Year 2 in M9 while the 1st annual progress report will be delivered in Year 2. INSERM will be responsible for the administrative, legal, and financial management, and compliance by Beneficiaries. The budget assignment is expected to be flexible in the framework of rolling AWPs to help in steering efforts in the most productive way. Thus, INSERM will coordinate the preparation of the financial part of the periodic Annual Progress Report and AWP. Furthermore, it will manage and coordinate any legal obligation such as Amendments to the Grant Agreement when required. In detail, **the activities of Year 1 will encompass:** (i) Management of the budget; (ii) Preparation and launch of payments to beneficiaries; (iii) Amendments (if required); (iv) Preparation and follow up of annual financial reports; (v) Financial support to beneficiaries. Lessons learned from the EJP RD will serve to further improve (already well-performing as acknowledged by the EC) financial follow up system (e.g. by implementing dedicated professional tools and their connection to the overall monitoring system).

ST1.1.3. Risk evaluation and mitigation *STL: INSERM_IT-GGB*
Risk evaluation and mitigation will be followed by the coordination team according to the initial risk strategy developed for each WP as well as inputs on the progress of activities provided during the meetings with the OG and ExCom. Furthermore, the monitoring system supporting the progress of the project (e.g. time to delivery or milestone achievement) will also be used to help in triggering relevant mitigation measures. Depending on the level of severity the implementation of mitigation measure may require prior discussion and validation of respective bodies (OG and/or ExCom for low and medium operational risks or GB for risks that may severely impact the whole project, e.g. breach by or withdrawal of a partner).

ST 1.1.4. Data Management Plan *STL: INSERM_IT-GGB Contributors: DDF*
The Partnership will gather and work with diverse types of data, which requires development of a comprehensive Data Management Plan (DMP) within the first six months of the project. The primary aim of the DMP is to ensure the accountability and reliability of the data, considering appropriate intellectual property (IP) protection and compliance with ethical rules, research integrity standards, FAIR principles, and GDPR regulations. Once finalized, the DMP will be reviewed and agreed upon and signed by all the Beneficiaries.
The DMP will encompass several key aspects:

- Handling of research data (and other outputs) during and after the project.
- Types of data to be collected.
- Application of data methodology and standards with input from the "Data Services Hub" stream.
- Modes of sharing and accessing data.
- Data curation and preservation.

The DMP will outline the scientific, technical, and organizational details for data and metadata collection, storage, retention, accessibility, privacy, confidentiality, destruction, quality assurance, backup, and resource allocation. It will comply with all relevant national and EU laws regarding the protection of personal data, and confirmation of compliance will be sought from all ERDERA partner organizations. The DMP will also include permissions to collect, use, reuse, and merge data from relevant authorities or primary owners/data controllers for activities such as T9.1. To develop the DMP, the Data Stewardship Wizard (DSW) will be used, which is a recommended planning tool by the Horizon Europe Program Guide. DSW allows for the assessment of the level of FAIRness of the research DMP, enabling continuous improvement in data handling throughout the Partnership and providing guidance to external users, thereby enhancing the reproducibility of research results. These improvements are crucial for successful collaborations with partners and effective IP management. The DMP will cover the management of Research, Development & Innovation data generated during activities related to ATMPs (Advanced Therapy Medicinal Products) development and manufacturing. This encompasses a wide range of data/output types, including target validation, engineering and profiling data, as well as late-stage product development data such as characterization, process analytics, and quality control (QC) testing. Additionally, new data will be generated/collected in the

context of performance assessment, capacity evaluation, infrastructure assessment of involved partners, use case/proof of concept studies, workshops, training/info sessions, scientific meetings, brokerage events, strategic meetings with stakeholders, and key performance and output evaluation. The Data Management Plan is expected as the D1.1 by the end of M6.

The generated data will adhere to ethical and data protection regulations, and efforts will be made towards digitalizing research activities, including the use of standardized digital tools for defining workflows and procedures, ensuring wide sharing and usability of research outputs across the consortium. To ensure explicit provenance and reproducibility, all records will be accompanied by supporting metadata based on the ISA metadata standard. Enriching the metadata with open ontologies provided by EBI's Ontology Lookup Service will be considered to optimize data interoperability. Electronic data/metadata will be stored on the ERDERA data platform for collaborative purposes, secure distribution, progress tracking, deliverable identification, and identification of IP potential. The DMP will also cover privacy by design and procedures to mitigate potential reverse engineering and unforeseen disclosure. The IT architecture will undergo risk assessment to ensure security, ethics, and privacy. Public content, such as public deliverables, workshops, training/info sessions, scientific meetings, and brokerage events, will be openly shared on the Partnership website. The DMP will be a dynamic document, regularly updated to incorporate inputs and evolution from engaged partners and the RD communities. The ERDERA will leverage partners' experience in projects with similar DMP requirements, particularly those involved in the Data services Hub stream, contributing to the EC's open science agenda by publishing FAIR Research Infrastructure data resources, making tools and workflows interoperable and reusable, and setting policies, specifications, and tools for data management in scientific research publications
The Partnership aims to establish an Open Innovation ecosystem that aligns with the Responsible Research & Innovation (R&I) goals set by the EC. Introducing Open Science practices as a standard for pre-competitive research endeavours will propel scientific progress while maintaining commercial potential to encourage further innovation in RD research and related R&I activities within the Partnership IP management strategy. The partners will collectively agree to incorporate Open Science processes and methodologies from the beginning through the Consortium Agreement. Once vital IP rights/interests, such as patents, patent applications, or protected know-how, are secured, the outputs (scientific publications, data, software, models, algorithms, monographs, conference proceedings, designs for materials, devices, and methods) will be made available through open access, adhering to the principle of "as open as possible as closed as (strictly) necessary." Publication of these outputs will undergo a comprehensive review process within the consortium, as agreed upon in the Consortium Agreement, to ensure confidentiality and protect the legitimate interests of all partners.

It is worth noting that private collaborators, who play a crucial role in the Partnership, might hesitate to participate in the innovation process if there is no intellectual property (IP) protection to safeguard their investments and market position. Therefore, while protecting IP rights is essential for new knowledge generated through translation and applied research to retain its commercial value, early-stage fundamental discoveries should be openly accessible to promote scientific advancement. Whenever feasible, the Open Research Europe platform will be utilized for publication, and efforts will be made to avoid paywalls in field-relevant journals by utilizing various publishing routes (green, gold, or diamond). Publications, including newly developed method protocols, will be shared at an early stage through pre-print repositories like BioRxiv to enable transparent feedback before journal submission. Prominent high-visibility journals in the RD field will be chosen to disseminate the research findings. Publications will be shared, promoted, and advertised on the Partnership website (through news feeds, blogs, newsletters) as well as on relevant social media platforms (Twitter, LinkedIn, etc.) to encourage future citations and enhance the global visibility.

To prioritize transparent disclosure and accessibility of data, processes, materials, and methods for use and replication by the broader research community, the Zenodo open repository and other specialized directories will be utilized. Scripts and codes generated throughout the research will be published on GitHub to facilitate systematic sharing and collaboration and promote the application of newly

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developed computational methods among the partners. Once fully developed, these scripts and codes will be made publicly available and, if applicable, compiled into open-source software for bioinformatics, such as Bioconductor. Other Open Science practices, including the early and open sharing of research negative outcomes and preregistration, will be assessed in the context of establishing an IP management strategy, working closely with WP2, to maximize the impact of the ERDERA.

T1.2. Governance & strategy (M1-M12) *TL: INSERM_IT-GGB; Contributors: TEAMIT, EURORDIS, GA UK*, HRCI, AFM, WDO, RDI.* T1.2. aligns with GO1-3; SO5; OO3,5.
The Governance and Strategy activities will be supported by a specific set of bodies as indicated in section 3.2 of the proposal. While the execution part will involve mostly the Coordination team, OG, ExCom, and General Assembly, the governance will be structured around the GB and the Board of Funders. The first one will provide the political and strategic steering within the frame of the Partnership to ensure coherence between Partnership activities and relevant European/national/international policies and priorities and facilitate the uptake of the Partnership results and outcomes and reflect on sustainability. The latter has a specific and "limited" role in the context of funding activities of the Partnership that are based on the provision of funding to third parties (Joint Transnational Calls, Networking support scheme and Clinical Trials Call). The strategic process will involve additionally the MAB and the National Alignment Board, the latter being specifically important for the implementation of measures related to the active participation of countries and widening measures.

To keep the Partnership on track while acknowledging the flexibility necessary to adapt its strategy to the evolving scientific and policy circumstances and to allow on timely deployment of revised agendas and activities, the governance and strategy driving processes must be dynamic and agile. This requires implementation of clear processes, tools and regular meetings to support the work of governing and strategy bodies.

The Coordination will assist in the constitution of all governing & strategy bodies by launching the official constitution processes, collecting nominations, providing terms of reference to newly selected members and storing confidential information. It is expected that all governing and advisory bodies should be established by M3.

ST1.2.1. Support to governance and advisory bodies *STL: INSERM_IT-GGB; Contributors: TEAMIT*
The Coordination team (INSERM_IT-GGB) will assist all governance and advisory bodies by providing the necessary tools (e.g., secured space for exchange and document storage, voting system), documents (required analyses, working documents, relevant drafts) and prepare the agendas. It will collaborate closely with the leaders of the Monitoring Task to provide regular or "on demand" updates on the performance of the Partnership or policy analyses that may support any strategic and/or policy discussions the GB of MAB would like to initiate. On the other hand, the Coo and executive bodies will have the possibility to propose subjects for discussion with the governing & advisory boards.

It is expected that the GB will meet at least twice during the 1st year and the MAB once every four months. **Within planned meetings the Governing Board shall meet in person at least once during Year 1**, among others, approve the AWP of the following year. Ideally, this in person meeting would be combined with the MAB and ExCom face to face meetings.

The organisation of the yearly in person meetings will be supported by TEAMIT. This will include identifying dates, selection of the venue, logistics, agenda preparation, contacting speakers, sending invites, minutes, etc. To ensure that national/EU activities, strategies, and needs are considered when taking decisions at the ERDERA level and when designing the AWPs, **the Coordination team will ensure that the National Alignment Board (NAB) will gather at least once during the Year 1.**

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To guarantee the agility and responsiveness, it is expected that the MAB, being the main advisory body of the Partnership, will be composed of a maximum of 20-25 external experts representing different types of stakeholders and horizons. However, when relevant, the consortium may request the assistance of MAB that goes beyond its core expertise. In such cases, the MAB will have the possibility to initiate the *Thematic Groups* and invite additional experts to advise on the requested topic. Some topics of interest have been already pre-identified as they are considered of primary importance to advance on some of the activities of the Partnership (namely clinical trials and therapy development):

- Addressing the challenge of underserved diseases areas (white spots) from a sustainability perspective by investigating the full development pathway. What can be improved or renewed within existing models to make development within these white spots more sustainable? What policy changes could occur to ensure investments in areas of higher risk. How may the partnership further facilitate the pathway to more sustainable models using its advantage of brining academia, industry, patients, and public funders as co-leaders?

The modalities for the recruitment of additional experts will be agreed by MAB. However, the model used in IRDiRC Task Forces, where open call for experts is published and final choice respects expertise, geographical and gender balance, could be an example.

In addition, if requested, the Coo will support the governing bodies (e.g. Board of Funders) in the organisation of public consultations to collect inputs on topics of relevance for the Partnership (and that require such input) e.g. calls for projects, key strategic orientations linked to the revision of the SRIA. This will be done in collaboration with the PPIE group to guarantee that the format, timelines, and response modalities are inclusive and adapted to people living with rare diseases.

Update of the SRIA

A structured and collaborative process will be implemented to ensure that the SRIA remains relevant, aligned with changing goals and priorities, and responsive to emerging challenges and opportunities. Stakeholders including, but not limited to researchers, patient representatives, policymakers, industry representatives and relevant experts will remain engaged in the SRIA Task Force and aligned through the organization of workshops, focus groups, and surveys to gather input on the current SRIA's strengths, weaknesses, and areas for improvement. The alignment with national, regional, and international research and innovation policies and strategies will continuously be sought with the help of the Governing Board.

A comprehensive analysis of the changing technological, economic, social, and environmental landscape will be conducted as part of the environmental scan, with the help of the MAB. It will seek to identifying emerging trends, challenges, and opportunities that may impact the SRIA's relevance and effectiveness. The SRIA will also undergo a SWOT analysis to identify gaps or shortcomings in the existing agenda that need to be addressed.

The review of previous performance will be accomplished through the assessment of the progress made on the goals and objectives outlined in the current SRIA version, using the ERDERA monitoring framework, identifying areas where targets were met, exceeded, or fell short.

Considering the insights from the above-described stakeholder engagement, environmental scan, and SWOT analysis, objectives may be added or updated to be made clearer and more measurable, and priorities would be defined based on the identified trends and challenges, focusing on areas with high potential impact.

The process of updating the SRIA will always consider alignment with funding sources and government policies as well as the agenda integration with relevant funding programs, grants, and initiatives.

The Partnership’s communication strategy will ensure the information of stakeholders about the

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updated SRIA, its goals, and the rationale behind the changes through various channels, such as websites, workshops, conferences, and publications. Moreover, a flexible and open feedback mechanism will be established to allows stakeholders to provide ongoing input and insights as the updated SRIA is implemented.

ST1.2.2. Patient and Public Involvement & Engagement (PPIE) *STL: EURORDIS; Contributors: GA UK*, HRCI, AFM, WDO, RDI*
Patient and public involvement, engagement, and participation (PPIE) is embedded in the WP Coordination to ensure that PPIE will be achieved throughout the ERDERA programme and governance structure, to ensure transparency, efficiency, patient-centricity and to make sure the Partnership research activities are - and remain - led by patients' needs. The PPIE group will encompass all representatives of participating patient organisations all over the ERDERA and will be supported by an operational team of patient organizations' representatives (with representatives from EURORDIS, GUK, HRCI, AFM, WDO, RDI). The rules of participation and mandate of the PPIE group will be defined by M2. The coalition of patients' groups and organizations involved in the ERDERA will rely on key principles such as accessibility, inclusion, diversity, and concertation.

The PPIE group will act as the advocacy arm of the Partnership to advance the cause of rare diseases research and improve patient outcomes. By M6, the PPIE group will have developed a framework for public & patient engagement encompassing all WSs. It will serve as a guidebook and be integrated in monitoring procedures. This will build upon existing frameworks, fostering already well-known established guidelines in PPI/PPE/PPIE and further refining any specific guidelines related to clinical research. During the first months (M1-M12) of the project, the PPIE group will support more specifically the following activities:

- Act as a hub to answer any questions or enquiry from patients not involved in the ERDERA.
- Collecting needs and expectations from patients' groups regarding the ERDERA.
- Identifying patients and patient representatives to take part in research tasks, proposals/project reviews and any other activities requiring a direct involvement of patients.
- Onboarding and supporting all patients and representatives involved in the Partnership activities by applying proven methodologies in engaging patients' groups in research and by building trusted patient partnerships in research.
- Providing a specific support to patients and patients' groups onboarding the CRNs as well as a continuous support to all patients' groups across Partnership activities.
- Linking all the aforementioned activities to the WP-Education & Training and vice-versa.
- Fostering links with patients' groups and networks who would benefit from the Partnership research activities (e.g. UDNI).
- In connection with the WP2 (Communication), developing any relevant resources for patient and families, regarding CRNs.
- Supporting the work of the coordination in developing surveys – when and if relevant - and engaging outside the Partnership's already established network.

T1.3. Monitoring of the Partnership activities (M1-M12) *TL: TEKKARE, CVBF; Contributors: INSERM_IT-GGB, ELS, MSW, CSO-MOH, ANR, FFRD, DLR, ISCIII, ZonMw, LMT, TEAMIT*. T1.3. aligns with GO1-3; SO5; OO3,5.
When monitoring the Partnership, effectiveness should be viewed as a non-linear, multi-faceted composite which changes in space and time. The monitoring activity to be developed within the Partnership must respond to several specific needs:

- At the level of the Partnership as a whole (level 1), the monitoring should enable the follow up of:
    - Specific KPIs: (i) KPIs defined within Horizon Europe for all funded projects and contributing to the Key Impact Pathways, (ii) Common indicators to be measured by all Partnerships and contributing to the Biennial Monitoring Report, (iii) KPIs defined in the Partnership's SRIA.
    - On demand analysis, especially related to the provision of information on participation

of /contribution of/benefit to individual countries.
    - Overall achievement of objectives and impacts.
- At the level of specific WPs (level 2) it should enable the follow up of WP performance (timely delivery, achievement of milestones, scientific and administrative performance, etc.).
- At the level of specific activities (level 3), for example: follow up of funded projects, of the networking scheme, trainings, outputs of the Technology Accelerator or the CRN, it should provide the tools for the follow up and analysis of results.
- At the level of the coordination (level 4), governance and strategy it should enable the collection and analysis of data required to support the decision-making processes and building of the sustainability plan by highlighting where and how value and impact are created.

The Monitoring Framework was defined during the preparation phase of ERDERA. It consists of 25 KPIs (9 short term, 10 medium term and 6 long term) linked to the ERDERA PSIPs with well-defined baselines, frequency and targets.
During Year 1, TLs will collect and analyse data according to the defined monitoring framework and based on the four level of monitoring:

Level 1 - ERDERA as a whole;
Level 2 - WPs performance;
Level 3 - monitoring of funded projects;
Level 4 - governance and strategy.

During Year 1, specific protocol for each KPI and their data needs will be designed in order to organize data collection (manual, automated, semi-automated. This work will result also in a list of components required to establish the monitoring system and a detailed work plan.

Validation of the Monitoring IT tool and processes will be performed.

ST1.3.1. Building the monitoring system *STL: TEKKARE; Contributors: ELS, INSERM_IT-GGB, CVBF, MSW Data Hub partners*
To respond to these needs, TEKKARE, jointly with contributing partners and in collaboration with other relevant WPs (e.g. Data Hub) will build the monitoring tools maximizing the use of pre-existing infrastructure, connecting to relevant APIs and products to provide a cost-effective and cost-efficient software to accelerate and automate the collection of monitoring data while minimizing technical and maintenance overheads. To this end, the monitoring system will be composed of the Back-office tools and purpose-oriented Monitoring Dashboards. For the back-office monitoring tools, the usage of open-source software Directus or similar to reduce cost for backend development will be privileged. It will also allow on easy integration of forms (surveys) and online reports with result data directly streamed to the back office. To ensure the most pertinent and useful collection of data and organization of metadata, TEKKARE will collaborate with Data Hub partners to design the most pertinent data model. It will also deploy streaming of Open data and TEKKARE technology (ref) to connect "internal" Partnership data (e.g. Microsoft graph - exploiting specific data of the Microsoft Teams collaborative platform, Data Stewardship Wizard) with "external" resources (like Elsevier dev portal, TEKKARE public data APIs and others) whenever contextualization in more global RD ecosystem is needed (e.g. compare the performance or provide external information to better define impact of the Partnership) to support decision-making and/or prioritization. Furthermore, to facilitate the monitoring and coordination of activities, GDPR-compliant technologies like posthog will be used to deploy digital activity monitors allowing on pre-automated, real-time data watch, analysis and generation of alerts.

The outputs of Partnership activities and their analysis that is processed and structured information based on the inputs generated from the resources mentioned above, will be exposed through an API for rapid development and visualization through dedicated (customised according to the users) Dashboards. To limit costs before developments and to initiate the project with high fidelity mock-up aligned with the user expectations on a User eXperience (UX), designer will be assigned by TEKKARE. The foreseen thematic Dashboards, guided by the Partnership needs collected during the

preparation of the programme, may include research papers, reports activity, country overviews, aggregations of online reports, clinical trials activity, etc.
The aim is to create awareness on the results and the progress of the Partnership; automate monitoring of the activity as much as possible with adapted tools while ensuring great user experience; and provide a sustainable framework with the set of monitoring tools to serve the RD research ecosystem. To this end, the design of the monitoring system will provide a sustainable model (brainstorming engaging future users to prototyping before development to avoid waste of efforts and means a flexible customization and deployment) for further expansion and creation of Knowledge Hub open to external users.

On year 1, TEKKARE will organize collection of Open Data that is helping to automate monitoring. More specifically TEKKARE will collect and organize clinical trials data and expose it through APIs to provide integration of this data into dashboards and reporting tools. TEKKARE will also deploy the monitoring portal on Year 1 after 3 months period prototyping it with the monitoring team to ensure it suits the need. The first dashboards will be deployed to the portal after the deployment of the portal is successfully tested (5-6 months after. Priority will be given on data that is already measurable and on tools that help collecting more data and create link between datasets: i.e. link a project from consortium to a publication / clinical trial or other.

On Year 1, TEKKARE will also create data model (entity relationships diagrams, data mapping, API specifications) and data flow diagrams necessary to automate and document the monitoring system. Dashboard and tool prototyping with high fidelity mock ups will be done also in order to align with stakeholders before any major development is done. Documentation will also be written in order to define how data should be collected for the different WP leaders in order to integrate successfully to the monitoring system. Actual development of the monitoring system, data pipeline, connectors will start on second part of Year 1. Connection with registration and participants forms data will allow to produce the first dashboard displaying the start of activity of the consortium.

ST1.3.2. Monitoring of Partnership's activities *STL: CVBF; Contributors: INSERM_IT-GGB, CSO-MOH, ANR, FFRD, DLR, ISCIII, ZonMw, LMT, TEAMIT, FTELE*
CVBF will support the coordination in the overall management of the monitoring activity and will be responsible for the monitoring level 1 (Partnership as a whole). This will encompass collection of data related to the pre-defined KPIs (see above), the analysis and generation of results in the form of processed data or (when relevant) reports. As stated above, CVBF will be supported by the extensive monitoring tools as well as by the coordination and all beneficiaries, whenever their input will be required to facilitate the collection of information.
For the Level 2 (WPs performance) the automation of the monitoring will be maximized by the integration of data flows from MS Teams collaborative tools and will serve the coordination, the OG and ExCom for efficient follow up and early risk management.

Level 3, being related to the monitoring of funded projects will be expanded beyond the monitoring system to ensure close follow-up and interaction with funded consortia. The monitoring of funded projects (from joint transnational calls and networking scheme) will be done by CSO-MOH and in collaboration with involved call secretariats from ANR, DLR, FFRD, ISCIII, and ZonMw. It will be carried out through online reports (provided through dedicated tool in the monitoring system) that will be filled out by the coordinators of the funded projects and reviewed at a midterm monitoring meeting in which experts will be invited to evaluate the progress of the funded projects. Each online report will be composed from the narrative description of the achievements and set of questions including specific indicators that will feed, among others, the main KPIs of the Partnership. The indicators, together with the reporting tool, will allow for follow up and monitoring of various aspects of the projects and the calls such as scientific progress, collaborations, RRI/ELSA measures, etc. In addition, a midterm monitoring meeting in which the coordinator (or another representative) of the funded consortia will present the progress of their projects, will be organized for each call. During the midterm meeting, the progress of the projects will be evaluated by scientific and patient experts who will provide feedback

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to the coordinators and the funders. It will be also used to facilitate the contact between applicants and all Partnership support services, including Data Hub, mentoring and accelerator services. r
All JTC funded projects of the ERDERA (and ongoing projects from EJP RD) will undergo follow-up and monitoring. **During the first 12 months** the following related tasks will be carried out:

- *Refinement and update of the monitoring process for the JTC funded projects.*
  A list of indicators was developed and applied to design the template for periodic and final reports of funded projects in the framework of EJP RD. The list will serve to establish and refine indicators for ERDERA-funded projects and adapted to fit the specifics of the JTC2025 call topic. Furthermore, the process of the follow-up and monitoring will be evaluated, as it has been done in EJP RD (considering the lessons learnt from the process done during the EJP RD timeframe) and adapted to be more efficient and suitable to suit the goals of this process in the ERDERA. An appropriate timeline will be set for the monitoring process according to the ERDERA JTC funding timeline and clear operating procedures will be defined. MSW will implement Polaris OS as a grant management platform for calls for projects and monitoring of funded projects. The platform will be customised (forms, workflows, interfaces, analytics...) to stick to the specifics of the project.
- *Follow-up and monitoring of EJP RD funded projects.*
  As a continuation of activities between EJP RD and ERDERA and important follow up of funded research, the monitoring of the ongoing projects from EJP RD will be continued during M1-M12 by collecting the annual and final reports from the unfinished projects that were funded under EJP RD calls: JTC2020, JTC2021, JTC2022 and JTC2023. The midterm monitoring meeting of JTC2022 will also be carried out during this period.
- *Analysis and mapping of the outcomes of the EJP RD JTC Calls and funded projects.*
  To understand the impact, sustainability, and exploitation of the results from the research supported by the JTCs funding activities and contribution to the RD field, it is important to perform the impact and exploitability analysis at the level of each call and each funded project. Granted networks grantees will have to complete a short online report within 2 months after their networking event has ended. These reports will be read, analysed, and used for communication purposes. During Year 1 of the partnership the process of the monitoring of the networking events will be refined and updated according to the many lessons that were learnt during the run of this scheme in EJP RD.

Finally, for the Level 4 (governance and strategy), it is expected that data integrated from other levels and complemented by external resources (mentioned above) will serve the coordination to generate information that will serve decision-making processes, support the needs of the GB and MAB, as well as help in feeding dissemination and communication actions (e.g. publication of contents summarizing the outputs/performance/impact) of the Partnership.

Resource Allocation will be monitored in WP1. The budget share contributing to each Operational Objective and mapped to Specific Objectives and General Objectives will be determined at the start of ERDERA. The resource allocated during the implementation of the Action will be monitored against performance (KPIs)
The Partnership Specific Impact Pathway (PSIP) links the Specific Objectives to the overarching goals, it results from the aggregation of links identified and agreed by the SRIA TF.

During Year 1, CVBF will collect data to monitor the Partnerships as a whole based on the defined Monitoring Framework. This will encompass collection of data, the analysis and generation of results in the form of processed data or (when relevant) reports. In close collaboration with TEKKARE, CVBF shall provide the monitoring data not automatically collected by the monitoring tool. As stated above, CVBF will be supported by the coordination and all beneficiaries, whenever their input will be required to facilitate the collection of information.
T1.4. Sustainability strategy (M1-M12) *TL: CE; Contributors: INSERM_IT-GGB, TEAMIT*. T1.4. aligns with GO1-3; SO5; OO3,5.
The sustainability strategy is a continuous process that encompasses both short-term and long-term

vision for the EU Institute for Rare Diseases. This means, on one hand, regular monitoring and provision of support related to the IPR and generation of any results that may require specific legal support and that will impact long-term sustainability. On the other hand, building the strategy and processes leading to future transition from the partnership to the sustainable institute with own legal status.

ST1.4.1. Support to IPR management and exploitation of results *STL: INSERM_IT-GGB*
In Year 1, as a first step the list of deliverables will be used to perform the necessary identification and quantification of joint results. This will result in an inventory of exploitable outputs that will be regularly updated. Results will comprise technologies developed, tools, services, as well as communication and training materials created and regulatory and standards guidelines which may constitute future services of the Institute. To ensure timely IP strategy management (complementary to the partners' tech transfer services) a dedicated support, provided by a small IPR support group composed of IPR experts of different partners, will be proposed (on demand) to facilitate the portfolio assessment. The group will be constituted by M6. This activity will be closely connected to the long-term sustainability sub-task as well as to the monitoring and communications to guarantee that exploitable results are properly acknowledge in sustainability planning and, whenever possible, openly disseminated.t
Furthermore, it is important to underline that partners will enter into a Consortium Agreement (CA), latest by the time of the start of the project (M1), which will address ownership, IP and access rights to Background and results of the project. Thus, the above outlined strategy will always be subject to conformity with the terms of such Consortium Agreement. The CA will specify the definitions of pre-existing knowledge and joint invention, the allocation of the IP rights associated to the results generated within the project, the rights for the partner entities and other entities such as their affiliates to use and/or exploit the results, as well as the rules governing publication and dissemination of the results and appropriate confidentiality terms. Based on usual practices in collaborative research, partners will define the IP policy to preserve their common and individual interests. Partners will share their intellectual resources and their background IP as needed for the implementation of the Partnership and for research use of someone's own results.

ST1.4.2. Long-term sustainability planning (phasing out) *STL: CE, Contributors: INSERM_IT-GGB, WDO*
The guiding principle is that the whole Partnership is greater than the sum of its parts, and the combination of specific services and activities constitutes the core added value of the Institute. Thus, in the first step, Copenhagen Economics, together with the coordination team and using input from the consortium and its advisory and governing bodies, will define the structured vision of the ERDERAs future entity. This vision will build on the findings of the Sustainability Report previously delivered for the EJP RD. Formulating the end goal at the beginning, will create a common goal that will be used as a guiding star for the workstreams and then annually updated as the project evolves.

In collaboration with the Monitoring and Strategy tasks, and IPR group, CE will use the inputs from the monitoring system, on progress of individual workstreams and results, to analyse the data to see where value is created and to provide advice to decision-makers on the evolution of the Partnership and possible reallocation of resources. Data driven decision making will increase the quality of decisions and improve success of the project as a whole.

The translation of the partnership to the final business case will be made based on the mapping of relevant business models and proposition of a most suitable legal setting (building on eBrains or EuReCA models) that corresponds to the federated nature of the future *institute*. The connections between each of the three services – support services infrastructure, CRN and support for research funding and calls - and the Partnership as a whole will be mapped from content and administrative perspectives. This will inform decisions about the place of each service within the *institute's* ecosystem and help in defining incentives and governance framework for its members, as well as financing

aspects.

The business case will need endorsement from the key stakeholders, including the EC and Member States. Demonstrating the achievements of previous partnership and documenting value and use cases of the future services will be critical to gain political support for the Institute. CE will support coordination team in this effort. **During Year 1,** CE will carry out the following activities:

- *Defining the long-term vision for the sustainable partnership.*
  CE will define together. with coordination team, using inputs from the consortium and its advisory and governing bodies, the structured vision for the sustainable entity. This will involve analysing factors that enable and inhibit future sustainability and proposing a monitoring system to help achieve the defined outcomes. This vision will build on the findings of sustainability report previously delivered for the European Joint Programme on Rare Diseases.
- *Monitoring the progress towards sustainability.*
  Building on the outcomes of discussions in point (1) above, CE will develop a method to analyse information and inputs gathered through the monitoring system to provide advice on the evolution of partnership towards sustainability.
- *Mapping of needs and business models.*
  The focus will be on existing data and knowledge sharing platforms such as eBrains, RDCA-DATA or EuReCA. CE will examine aspects such as the incentives framework, technological solutions, governance, and legal entity types. This activity will continue in the second year, and the results will be presented to and discussed with the governing boards and ERDERA partners.

T1.5. Ethics compliance (M1-M12) *TL: FGB; Contributors: INSERM_IT-GGB.* T1.1. aligns with GO1-3; SO5; OO3,5.
To guarantee and support ethics compliance of all project activities, an internal Ethics Advisory Group (EAG) will be set up in Year 1 and composed of 3-5 ethics experts delegated by beneficiaries. At least 1 patient representative will be part of the group. All the activities to set up the support on ethics issues/concerns raised during the implementation of ERDERA's actions and its research activities will be initiated. This will include the ethics assessment and/or follow-up of funded projects. Different ethics aspects will be addressed according to the Horizon Europe ethics guidance including but not limited to animal welfare, research with humans, data processing activities, involvement of children, AI methods, etc. Bimonthly remote meetings and an in-person meetings (M12) will be scheduled in **Year 1**. This model has been already successfully implemented in EJP RD. Moreover, according to the provisions from the European Commission, an Independent Ethics Advisor (IEA) will be appointed.

Additional deliverables *(additional to those included in part B of the proposal)*
None

Set of Activities Number	**2**	**Start Date or Starting Event**	**M1: September 2024**
Set of Activities Title	**Communication & dissemination**		
Short name of participant & (No)	TEAMIT (2)		
Person Months	24		
Start month	M1	**End month**	M12

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State of the art behind this WP

ERDERA's communication strategy is firmly rooted in the foundation laid by the European Joint Program on Rare Diseases (EJP RD). The European Joint Programme on Rare Diseases is recognised for its efficiency and its impactful approach to communication, and ERDERA recognizes the value of continuing and expanding upon this tradition. ERDERA WP 'Communication,' is thus aligned with the communication strategy of EJP RD (EJP RD WP5 “Communication & Dissemination”).

One of the main goals of the EJP RD WP5 is to communicate and disseminate the work from each EJP RD Pillar and EJP RD itself as a whole. In order to showcase the output of the work done, elements such as news, events, workshops, or publications were developed as the main items used for dissemination. Different tools have been used to communicate and disseminate outside from the consortium including the EJP RD website, social media, newsletters, videos, and a mailing list of communication managers’ network that continue to be maintained and developed. In addition to these tools, contribution to events such as the RE(ACT) Congress & IRDiRC Conference has fostered the dissemination of the EJP RD activities and achievements. The communication and dissemination capacity at regional and national level have been considered as a high priority during the EJP RD lifetime, leveraging on EJP RD partners’ potential to vehicle unified information and multiplying the outreach spread.

By building upon the successful communication framework established by EJP RD and working closely with the same coordination team at INSERM, ERDERA communication team at TEAMIT ensures that its communication efforts are not only in line with its parent program but also positioned to make a significant impact in advancing rare disease research and collaboration across Europe and the world. This alignment not only strengthens the ERDERA partnership but also bolsters the broader efforts to address rare diseases on a continental scale.

Methodology

Structured communications (C) and dissemination (D) activities are key to pave the way for future sustainability of results and outcomes generated by ERDERA. This requires of a sound C & D strategy that aligns with the Partnerships goals and appropriately targets all key stakeholders that either benefit, use, interact and/or shape in varying degrees the RD ecosystem. Beyond carrying ERDERA’s voice to the outside world, WP2 contributes to inform and construct compelling value propositions to ensure, going forward, the acceptance and uptake of outcomes, thus maximising the impact of ERDERA. With this end goal in mind, the C&D strategy will seek to:

1. Generate awareness on the new Partnership, whilst continue raising interest in results, services and tools already made available by EJPRD.
2. Spark attention on activities, calls and new results and resources developed by ERDERA.
3. Ensure broad understanding of the impact of RD on patient’s family and society.
4. Amplify dissemination and acceptance of research outputs, highlighting their soundness, relevance and potential impact.
5. Facilitate stakeholder engagement that results in meaningful interactions and fruitful international collaboration.

WP2 will follow a persona approach to develop, through surveys, interviews and focus groups, detailed empathy maps for each audience segment. These will be the basis to design tailored strategies and messaging that addresses concerns and conveys clear value propositions. The proposed communication mix ensuing the audience analysis will propose specific strategies for each stakeholder segment and recommend appropriate channels, tools and activities depicted below:

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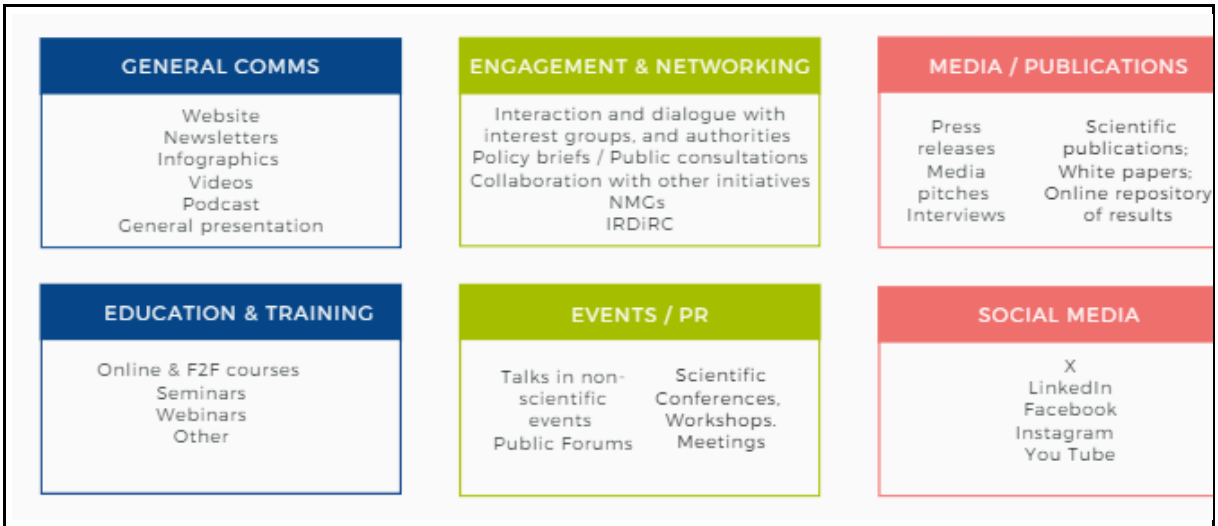


Figure 6

WP2 will pay special attention to case studies and stakeholder testimonials and will showcase them employing storytelling techniques, whenever possible. So, it will observe basic principles of communication (Rhetoric, Aristotle), ensuring credibility (ethos) by involving key opinion leaders and authoritative voices on the RD field, empathy (pathos) by showcasing personal stories and logic (logos) by presenting facts and corroborated scientific evidence. It will apply science communication best practices to facilitate understanding and usefulness (i.e., avoid jargon, provide examples, summarise ideas, contextualise, start with key findings, etc).

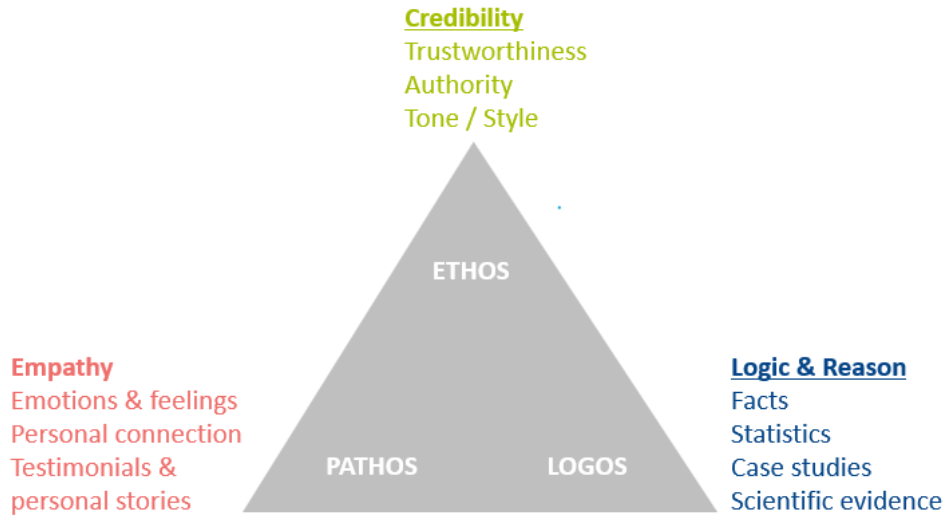


Figure 7

Objectives

In its Year 1, WP2 will focus on:

- Developing ERDERA's brand and raise awareness about its vision and mission, continuing the process initiated by EJP RD of positioning this ambitious programme, as a pivotal actor to advance RD research and build the RD ecosystem in Europe and beyond.
- Designing a communication and dissemination (C&D) strategy by M6 that builds on EJP RD and supports long-term ERDERA's objectives.
- Construct a coherent narrative across the whole partnership through the development of a set of key messages (general and audience specific) and an editorial plan that are embedded into the C&D strategy.

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- Promote available resources, partnership's activities and calls; communicate progress made in Year 1 and disseminate results to build ERDERA's reputation as an enabler of innovative, standardised, streamlined, and collaborative transnational RD research.
- Support all WPs in their communication needs in Year 1, facilitating the necessary tools and materials and ensure consistency and alignment with the overall communication strategy and plans.
- In collaboration with all WSs and partners' comms representatives, maximise outreach and contribute to foster engagement, knowledge exchange and community building.

Description of Programmed Activities

T2.1. Communication and dissemination strategy (M1-M12) *TL: TEAMIT, INSERM_IT-GGB.* T2.1. aligns with GO:3; SO:3,5; OO:3,5.
This task will build on EJP RD achievements to design a sound communication (C) and dissemination (D) strategy for ERDERA by M6, tailored to specific audience groups. This strategy will observe Open Science principles and support and enhance ERDERA's overall objectives and its position in the ecosystem as a global enabler of strategic and impactful research. A comprehensive audience analysis, initially informed by representatives of all WSs and partners' communication experts, will constitute the backbone of the C&D strategy. This will be led by the senior communications manager and will include:

- A communications SWOT analysis that incorporates learnings, achievements, and resources from EJPRD.
- An audience analysis to identify needs, motivations, attitudes, and desired communication objectives following a persona approach. This will serve as a basis to generate future value proposition canvas. Considering the broad scope of ERDERA and the many tasks undertaken, this audience analysis exercise will be conducted for each WS. As stakeholders' motivations and needs to be fulfilled by each WS may differ, the subsequent strategies and messaging will need to reflect these nuances and be tailored; accordingly, these empathy maps will be reviewed on annual basis to reflect any shifts in attitudes and needs as the partnership and the RD research ecosystem moves forward.
- Clear C&D objectives for each audience group.
- A set of key messages (generic and specific for each audience group).
- Mapping of audiences to match them with appropriate communication channels and tools (communications matrix).
- Specific KPIs to feed into T1.3 for regular evaluation of C&D strategy performance.
- Explicit roles and responsibilities.

The first 6 months of the project will focus on the development of this C&D strategy. As previously described, WP2 will first analyse results from the C&D strategy implemented by EJP RD this past 5 years to extract learnings, identify gaps and continue building on what has already been done and proved successful. A second critical task will involve building/refining empathy maps for the following audience groups:

1. **RESEARCHERS**
   - **ERDERA funded initiatives**
   - Academia*, clinical and/or clinical researchers
     - Systems Biologists
     - Data scientists
     - Biobank managers
     - Laboratory scientists & technicians
     - Clinical geneticists
   - Research organisations
   - Learned societies
   - Professional associations (i.e., CGCOM; CENOM)
   - Applicants to ERDERA funding calls
   - Academic institutions/Universities

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- Medical & biomedical students
  - Lecturers
  - University managers
  - Organizations of academic institutions (i.e., UEMS)

2. **PATIENTS**
   - Patient organisations
   - Patients & care givers
   - ePAGs (RD patient representatives involved in ERNs)
   - YPAGs (Young Patient Advisory Groups)
3. **PUBLIC DECISION MAKERS**
   - **National Mirror Groups (NMGs)**
   - Ministries of Health & Research
   - European Commission (EC)
   - Relevant EU directorates (DG RTD, Santé, Connect)
   - (Funding) Program directors and managers
   - National legislators focused on health and research
   - European legislators focused on health and research
4. **OTHER CONSORTIA & ASSOCIATIONS**
   - IRDiRC
   - ESFRI
   - Other research initiatives
5. **REGULATORS & HTAS**
6. **FUNDERS**
   - Philanthropic organisations
   - (Inter)national public funding bodies
   - Venture capital
7. **INDUSTRY/PRIVATE SECTOR**
   - Large pharmaceutical companies
   - SMEs / Biotech
     - Pharma, medical devices, ATMPs; ICTs
     - EFPIA; EUCOPE
     - Innovation managers
8. **RESEARCH INFRASTRUCTURES**
   - ESFRI
9. **HEALTH CARE PROVIDERS**
   - European Reference Networks (ERNs)
   - EUHA
   - Hospitals/Clinicians at large
10. **GENERAL PUBLIC**
11. **MEDIA**

Surveys and focus group interviews will be conducted from M2-M4 to gather meaningful insights into each audience group. To this end, WP2 will reach out to ERDERA WS leaders to help identify partners' spokespersons who can offer an in-depth overview on needs, motivations and attitudes of key stakeholders. This exercise will allow to construct empathy maps that include specific communication objectives, strong messaging and value propositions. These will not only inform the C&D strategy but also future sustainability plans. Based on these empathy maps, WP2 will develop the C&D strategy and an initial calendar of activities covering M6-M12. The proposed strategy will be presented for approval to the Executive Committee by M6 before submission of Deliverable D2.2 ("Communication and dissemination strategy"). The D2.1 will be developed by M3 "Project website»

T2.2. C&D operational plans (M1-M12) *TL: TEAMIT, INSERM_IT-GGB.* T2.2. aligns with GO:3; SO:3; OO:3,5.

This task will implement the approved strategy through AWPs designed with the concurrence of WP leaders and based on the analysis of the performance evaluation conducted in WP1. These will include SMART communication objectives, operational pillars or a pre-emptive calendar of activities, audience specific. T2.2. will also develop an editorial plan that constructs and supports a coherent ERDERA narrative to convey its role in driving innovation, collaboration and international alignment for cutting edge RD research. This will be led by a scientific writer capable of communicating complex concepts and results to all types of audiences, using whenever possible, case studies, personal testimonies, etc. Of note, the scientific writer will not contribute to the production of scientific publications, blueprints, reports, etc which are the responsibility of each WP but will support their dissemination once available. Finally, T2.2. will be responsible for the implementation, coordination with partnering organisations and monitoring of communications plans and will collect quarterly KPIs for subsequent evaluation. A communications officer with expertise on digital channels will also support the successful delivery of planned activities.

Before the new partnership officially starts, WP2 will prepare a tactical communications plan to announce/launch the new partnership ERDERA, successor of EJP RD. Tasks will include:

- Develop new branding & adapt channels (website, social media, etc) accordingly.
- Based on DoA, construct basic messaging to:
    - Present ERDERA as the successor of EJP RD which will build on its experience and achievements to continue advancing cutting-edge transnational RD research and building a strong ecosystem in Europe and beyond.
    - Convey ERDERA's vision and mission, as a continuation/progression of EJP RD
    - Highlight kye changes/novelties in relation to EJP RD
    - Outline strategy/work plan
- Draft press release and design a coordinated distribution plan.

These specific activities will be depicted in milestone M2.1 ("Initial set of tools and activities").

Whilst transitioning from EJP RD and developing ERDERA's C&D strategy (T2.1), T2.2 will carry out communication activities and will progressively implement and monitor communications and editorial plans with a pre-emptive calendar of activities that will include:

- At least bi-weekly posts on LinkedIn, X, Facebook, and Instagram, raising awareness on rare diseases impact and current status quo in research, generating interest about ERDERA's objectives and its expected impacts and, concurrently with T2.3, promoting partnership's activities (incl. joint calls) and available tools, resources and services.
- A quarterly newsletter informing of WSs activities in Year 1; showcasing partnership's progress and highlighting future activities. The subscription form will allow to indicate topics of interest and type of audiences to allow future segmented newsletters.
- Weekly website updates with dynamic content (news, events, etc).

T2.3. Synergies with WSs and communication tools (M1-M12) *TL: TEAMIT; Contributors: INSERM_IT-GGB, EURORDIS, WDO, FFRD, TEDDY.* T2.3. aligns with GO:3; SO:2,3,5; OO:3-5.
This task will leverage channels, tools and resources generated by EJP RD to further refine ERDERA's branding and communication platforms and materials (website, newsletter, videos, infographics, factsheets, social media assets, etc) to support the Partnership in all communication and dissemination needs. This transversal WP will synergise with all WSs to aid understanding of their objectives, ongoing work plan and relevance of results generated by each of them. **It will also promote services, resources and tools and disseminate any new knowledge produced during Year 1.** More specific actions to be implemented in collaboration with WSs by M12 are as follows:

Coordination

- An infographic depicting SRIA (T1.2) to generate awareness and understanding around RD policy research strategies, regulatory, legal and ethical issues and the role of ERDERA.

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- Consultation with T1.4 to generate the empathy maps (M2-M6) and initial value propositions and ensure alignment with future exit strategy.
- Downloadable factsheet addressed specifically to patients, families and society in general describing current status quo in RD research and the positive impact ERDERA aims to deliver.
- Patients section on ERDERA's website to include by M12 written articles on patient engagement and a video interview with a patient representative.
- Fixed newsletter section offering patients' perspective in a number of RD research topics.

RD Funding

- Tactical communications plans to promote first and second funding calls, as well as webinars for candidates & public consultations through all available channels (ERDERA and its partners or other consortia and initiatives) and to inform, as well of calls' results (M12) and the expected impact of funded research projects. This will include a mix of channels (website, social media, flash newsletter) and tools (banner, videos, etc).
- Dedicated website section signposting to new calls and including information on past calls and already funded research.

CRNs:

- Dedicated website section promoting, in an engaging and visual manner, available services, tools and resources.

Data Services Hub

- Infographic to aid promotion of the virtual platform and signpost accessible services and newly onboarded resources available through main website in a section dedicated to RD research data.
- Regular dissemination through the website and social media of any new knowledge generated on genetic cause of diseases, to aid the adoption of methods that increases the usability of rare disease data.

Expertise Services Hub

- Social media campaign to promote the Innovation Management Toolbox and signpost any new resources as they become available.
- Newsletter article including a user testimonial of mentoring, consultancy or methodological support services and the Regulatory Support Group.

Education & Training

- Infographic signposting to training resources and educational activities.
- Social media campaign and e-mail updates targeting (inter)national organisations (NGOs, learned societies, universities) to promote resources and activities.
- Fixed newsletter section publicising latest trainings and promoting future events.

Acceleration Hub

- Dedicated section on website signposting to the future innovation marketplace; depicting case study/ies or most promising projects (i.e.; project of the month) and promoting matchmaking activities.
- Fixed newsletter section showcasing mots advance/promising projects or promoting a key activity or event.

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- Social media campaign to encourage potential investors to follow and engage with ERDERA.

Inter(national) Capacity

- Fixed website section dedicated to NMGs featuring stories on selected activities, good practices and achievements to highlight their value in ensuring cross-fertilisation, knowledge transfer and alignment.
- Fixed section on general newsletter and bi-annual specific newsletter addressed to NMGs.
- Guidance on the design of their annual communications plans. Amplify dissemination of IRDiRC key activities (state of the play; annual meeting; etc) through ERDERA channels and media outreach.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**3**	**Start Date or Starting Event**	**M1: September 2024**			
Set of Activities Title	**Joint Transnational Calls for collaborative research projects**					
Short name of participant & (No)	DLR (3)	ANR (4)	FFRD (29)	ISCIII (72)	EURORDIS (26)	FTELE (5)	IFD (59)
Person Months	14.75	3.25	1.75	1.2	1.0	0.75	0.75
Short name of participant & (No)	WDO (120)	ETAG (100)	F.R.S.-FNRS (54)	FCT (61)	FNR (138)	FRRB (56)	FWF (58)
Person Months	0.2	0.75	0.75	0.75	0.75	0.75	0.75
Short name of participant & (No)	FWO (92)	HRB (67)	Rannis (69)	IT-MOH (76)	LMT (6)	LZP (78)	MOSAE (103)
Person Months	0.75	0.75	0.75	0.75	0.75	0.75	0.75
Short name of participant & (No)	NCBR (83)	RCN (91)	RIF (94)	SAS (101)	SPW (98)	SRC (104)	RT(TuscReg) (109)
Person Months	0.75	0.75	0.75	0.75	0.75	0.75	0.95
Short name of participant & (No)	UEFISCDI (126)	Vinnova (144)	CSO-MOH (49)	TÜBITAK (108)	MUR (82)	ZonMw (7)	NKIFH (139)
Person Months	0.75	0.75	0.75	0.75	0.75	1.45	0.75
Short name of participant & (No)	BMBF ** (41)	CIHR* (153)	FRQS* (156)	DFG* (154)	SNSF* (166)	BNSF (129)	AZV (62.1)
Person Months						0.75	0.75

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Short name of participant & (No)	MZd ** (62)		
Person Months			
Start month	M1	**End month**	M12

**Associated partners providing in-kind contribution*

*** Beneficiaries providing in-kind contribution*

State of the art behind this WP

Notwithstanding the important progress in the Rare Diseases (RD) field, many aspects remain without solutions. The need for fundamental, translational, clinical, social and health services research and most efficient modes of fostering them are therefore still topical. Since at present, only few European countries fund research on RD through specific dedicated programmes, the funding of transnational collaborative research is the most effective joint activity to enhance the cooperation between scientists working on RD in Europe and beyond, and thus reducing fragmentation of research in this field. These funding opportunities will be built on the positive and longstanding experience of E-Rare and EJP RD.

Methodology

The WP will implement patient centric transnational and collaborative research among scientists, clinicians, companies, and patient organisations, with the goal of reducing the burden of rare diseases (RD) for patients in Europe and beyond. This includes appropriate mechanisms for relevant topic selection (pre-identifying gaps from past calls and including innovative subjects), wide participation of outstanding teams and engagement patients and research teams from underrepresented countries in the whole process. Transnational calls will cover topics of interest for patients, obtaining an accurate diagnosis, developing new therapies, and improving the life of patients by funding projects ranging from basic to pre-clinical, clinical and implementation/translational research, to human and social sciences and interdisciplinary research. Seven joint transnational EC co-funded calls (JTCs) should be launched with an estimated overall budget of more than about 150 Mio. €. Parts of the EC co-fund budget will be dedicated to funding patient advocacy organisations (PAOs) involved in research projects. The applicants will be linked to the Partnership services concerning translational mentoring, regulatory support, and data management during the application process to benefit from cross-disciplinary expertise and goal-oriented study planning. This will be further supported by targeted training opportunities. This will enable efficient execution that feed into innovation and facilitates uptake of results through opportunities presented in the acceleration hub. The WP contributes to all ERDERA objectives and is linked to all WPs.

Objectives

The funding of transnational collaborative research is critical to enhance the cooperation between scientists working on rare diseases across Europe and beyond. Therefore, the main goal of this WP is to implement seven joint transnational EC co-funded calls which include the following tasks:

- Topic selection and definition of eligibility criteria
- JTC call implementation
- Engagement of patients.

Transnational calls on diagnosis, therapy development, improved understanding of clinical outcomes or SSH research will be launched over the 7 coming years. **In Year 1**, the first call will be launched, the second call will be prepared and the patient engagement working group will be set up.

Description of Programmed Activities

First joint transnational call

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T3.1. Call topic selection for JTCs and Clinical Trial Calls (M1-M12) *TL: ANR, DLR, ISCIII, FFRD, FTELE; Contributors: ZonMw, WDO, EURORDIS, all participating funding agencies (BMBF, BNSF, CIHR, CSO-MOH, DFG*, ETAg, F.R.S.-FNRS, FCT, FNR, FRQS, FRRB, FWF, FWO, HRB, IFD, IT-MOH, LMT, LZP, MOSAE, MUR, MZd, NCBR, NKFIH, Rannis, RCN, RIF, RT (TuscReg), SAS, SNSF, SPW, SRC, TUBITAK, UEFISCDI, Vinnova)*. T3.1. aligns with GO:1-3; SO:1-5; OO:1-5. A centralized process for the identification of topics for the joint transnational and clinical trial calls will be established and include multi-stakeholder input from the rare disease community inside and outside the partnership as well as IRDiRC and lessons learned from previous E-Rare and EJP RD calls. It is envisioned to formulate a multi-annual call topic strategy with broader themes which will be developed in consultation with the ERDERA MAB together with ad hoc advisors and then opened to public consultation. Further refinements will then be made for each topic by the Board of Funders. The topics and call procedures will be submitted in advance to the EC for validation.

To maximize synergies, it is expected that the topics for the first three joint transnational calls will be in line with the CRN themes diagnosis, therapy development and improved understanding of clinical outcomes. Themes in years 4-7 will take advantage of ATMP technology advancement knowledge derived from WP11 and WP21 as well as facilitate early career researchers or human and social sciences research among other possible themes which will be closely linked to the developments in the CRNs and accelerator hub. It is foreseen that the clinical trial topics will focus on RD not yet treated and not investigated by enterprises. **In Year 1,** the topics for the first and second joint transnational call as well as the topic for the clinical trial call will be developed.

To avoid conflicts of interest, a strict firewall between the parties deciding on call topics and partnership beneficiaries will be established. This includes:
Phase 1: Open general topic definition (see description above)
Phase 2: locked and involving only participating funding organisations: decision on the choice of topic (if several proposed) and/or refinement of topic details, eligibility rules, etc.

- In the case of involvement of experts from outside the partnership or from participating RPOs in these processes the participation of these experts to the call (as well as participation of their direct collaborators) is forbidden. Each expert signs a confidentiality clause.
- Decision on topic description and call documents made solely by representatives of funding bodies.
- Mentioning of call topic in partnership boards only in broadest terms (e.g., focus on diagnosis, therapy development).
- Persons and their direct research groups that participated in activities above are not allowed to apply for funding.
- Detailed call topic description will only be made available outside the Board of Funders through publishing of the public call documents (pre-announcement, call publishing).
- If organizations are both Research Funding Organisations (Programme Manager) and Research Performing Organisations (e.g., INSERM/ISCIII/FTELE) additional measures are put in place to enable eligibility RPO parts of these organisations to apply to the call:
    - nomination of dedicated persons to represent above institution in topic selection process who cannot apply to call.
    - any other person from INSERM/ISCIII/FTELE participating directly or indirectly (through the possible third parties) in the partnership are not involved in: decision on topic of the call; the description and preparation of call documents; the preparation of the pre-announcement; the call evaluation process; the final decision on the projects to be funded.

In the topic description of the call, a list of excluded (sub)topics or disease areas dependent on initiatives that take place inside and/or outside the partnership will be elaborated. The final validation of topics will be taken by the Board of Funders in close collaboration with the EC.

T3.2. JTC implementation (M1-M12) *TL: DLR, ANR, FFRD, ISCIII; Contributors: all participating funding agencies (BMBF, BNSF, CIHR, CSO-MOH, DFG*, ETAg, F.R.S.-FNRS, FCT, FNR, FRQS, FRRB, FTELE, FWF, FWO, HRB, IFD, IT-MOH, LMT, LZP, MOSAE, MUR, MZd, NCBR, NKFIH, Rannis, RCN, RIF, RT (TuscReg), SAS, SNSF, SPW, SRC, TUBITAK, UEFISCDI, Vinnova, ZonMW).* T3.2. aligns with GO:1-3; SO:1-5; OO:1-5.

ST3.2.1. Preparation of the first joint transnational call and establishment of the joint call secretariat *STL: DLR; Contributors: all participating funding agencies*
The TL will be responsible for facilitating the definition of eligibility criteria for the call. The following criteria were used in past calls but will need to be adapted to the specifics of the call topic and the lessons learned from previous calls:

- Only transnational projects will be funded.
- There will be a minimum and maximum number of partners per proposal.
- No more than two eligible partners from the same country participating in the call will be accepted in one consortium.
- The consortium coordinator must always be eligible to receive funding from the funding organisations participating in the call.
- Although applications will be submitted jointly by research partners from several countries, individual groups will be funded by the funding organisation of their country/region that is participating in the call. Applications are therefore subjected to eligibility criteria of the involved individual funding organisations.
- Enlargement options for consortia will be used to incentivize inclusion of partners from underrepresented countries or early career researchers. The inclusion of partners from underrepresented countries (widening measures) will be further facilitated through close collaboration with WP24.
- To facilitate the participation of patient groups in the proposals, a dedicated budget will be set aside to support their tasks in the projects.

Depending on country/regional regulations, joint research proposals may be submitted by applicants belonging to academia, the clinical/public health sector, enterprises, or private not-for-profit organisations (e.g. patient organisations, foundations, etc.). Although no limit will be set for a maximum grant amount, it is expected that consortia will apply for budgets aligned with the proposed research activities planned for a maximum of 36 months. Moreover, national budget limitations may apply.

The TL will be responsible for drafting and finalizing all necessary documents including:

- Memorandum of Understanding
- Call text
- Governance and evaluation procedures
- Guidelines for applicants
- Proposal templates
- Other documents that might become relevant

Previous versions of these documents already established in the first EJP RD and validated by the Commission will efficiently be used as example templates and then adapted following comments made during EJP RD calls. In addition, the TL will set up the JCS which will act as central support to the applicants regarding all aspects of proposal drafting and submission. Finally, each participating funding organization will establish its national/regional contact point. Potential applicants will be strongly encouraged to contact their national/regional representative for advice on national/regional rules and regulations, including eligibility and financial budget regulations.

The call for proposals will be published on the ERDERA website and by relevant national/regional funding organizations via their national publishing routines such as websites, newsletters, press announcements, etc. The publishing instruments of the EC, such as the Participant Portal and ERA-

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LEARN, will be used as well. If feasible, a call pre-announcement will be published to maximize the early mobilization of the RD research community. The call will be opened for the submission of proposals for at least 60 days. A webinar will be held to inform applicants of the call specifics. The TL will be supported in the implementation of all steps by a JTC operating group consisting of representatives of all JCS implementing organisations.

ST3.2.2. Scientific evaluation of the first joint transnational call STL*: DLR; Contributors: all participating funding agencies (M3-M12)*
The evaluation will be implemented in a two-step procedure according to the Horizon Europe rules. In the first step, applicants are invited to submit pre-proposals, which describe a short outline of the proposed work. The eligible applications will first undergo national eligibility check and then be submitted to the transnational peer review Scientific Evaluation Committee (SEC) composed of independent expert scientists chosen for their scientific, technical and/or disease-specific expertise, as well as patient representatives. The Committee will be as far as possible gender and geographically balanced, including experts from countries participating and not participating in the call, experienced (i.e. previous SEC members) as well as new members. Reviewers will be carefully selected regarding any potential conflict of interest. The evaluation of proposals will be aligned on the scoring system and criteria ('excellence', 'impact' and 'quality and efficiency of the implementation') of Horizon Europe. The SEC will select the most promising applications for submission of a full proposal. The tentative number of proposals retained for the second step will be about 2-3 times the number of possibly funded projects and will depend on where a break is perceptible in the quality of proposals.

The full proposal step will be used to facilitate inclusion of additional partners from underrepresented/undersubscribed countries through a voluntary widening step. Applicants will be able to receive advice on ethical, regulatory, innovation, translational and data management aspects from partnership services (WP 17, 18, and 19) and can modify their proposals accordingly. In the second step of the evaluation, the JCS will check the submitted full proposals to ensure that they meet the call formal criteria. Subsequently, the submitted full proposals will be reviewed by three members of the previously established SEC. These will be complemented by patient experts and methodological experts. In a second meeting the SEC will agree on a final ranking list of excellent proposals recommended for funding. The consortium will take all lawful steps to ensure confidentiality of information and documents obtained during the evaluation and selection procedures of the joint call. In addition, an independent expert will be invited as official observer to the second SEC meeting to assess the conformity of the general implementation of the joint call and specifically the proper implementation of the international peer review and establishment of the ranking list of transnational projects. The assessment of the observer will be provided in a report to the European Commission. It is expected that the evaluation process including provision of written evaluation reports will be finished in M15.

A clear link to the ERDERA services regarding translational mentoring and data management will be established. The requested budget in the proposals applying to the JTCs should already include provisions to allow funding of these services to deliver on the ERDERA mission that "every high-quality project will benefit from cross-disciplinary expertise, goal-oriented study planning and efficient execution". This will be considered when defining mechanisms driving different steps of JTC application and evaluation in more detail.

ST3.2.3. Ethics evaluation of projects recommended for funding of the first joint transnational call *STL: DLR; Contributors: all participating funding agencies.*
An ethics evaluation of the projects selected for funding will be done by independent ethics evaluators following Horizon Europe standards. Applicants will be obliged to comply to ethics requirements delineated by the ethics evaluators. Only projects that pass the ethics evaluation will be funded. The follow up of ethics compliance of all funded projects will be done in collaboration with WP1. The process will be started in M6 with the selection of ethics experts suitable for the topic of the call and

is expected to finish in M14. The follow-up of the ethics evaluation results will be done in the relevant tasks in WP1.

ST3.2.4. Funding decision of the first joint transnational call *STL: DLR; Contributors: all participating funding agencies*
The CSC will take its final funding decision based strictly on the scientific recommendation of the SEC (ranking list). As many full proposals as possible with a clear funding recommendation will be funded, considering the available budget. Each eligible applicant will be funded by the organization of the country/region from which the applicants have applied and according to the national/regional administrative regulations (virtual common pot model). This will be done in accordance with the general criteria fixed in advance to the launch of the call to avoid the underestimation of national/regional budgets. If proposals have identical scores, the proposals coming from participating organizations with still available funding will be given precedence, to further maximize the number of selected projects. The joint selection list of projects to be funded will be communicated to the EC. The applicants will be informed about the final funding decision and the national negotiations will commence. The final funding list will be prepared by the JCS and provided to WP2 leader for publication on the partnership communication channels as well as the relevant EC portals. The process will be started on M12 and is expected to finish in M15. Monitoring of the funded projects will be implemented through WP1 in year 2.

Second joint transnational call

T3.1_(2). Topic selection for the second joint transnational call (M3-M12) *TL: ANR; Contributors: FTELE, ZonMw, WDO, EURORDIS, all participating funding agencies*

T3.2_(2). Joint Transnational call - implementation of the second call (M6-M12) *TL: ANR; Contributors: all participating funding agencies*

ST3.2.1_(2). Preparation of the second joint transnational call and establishment of the joint call secretariat *STL: ANR; Contributors: all participating funding agencies*

In general, the description of work for this call is analogous to the first call described above. Lessons learned from the first call and strategic input from the other WPs will be considered for all the steps included in this call.

T3.3. Engagement of patients in research project funding (M1-M12) *TL: EURORDIS, FFRD, DLR; Contributors: ANR, ISCIII, ZonMw, RT (TuscReg), WDO, AFM.* T3.3. aligns with GO:1-3; SO:1,3-5; OO:1,4,5.
The working group will be composed of both funders and representatives of RD patients. It will focus on improving patient involvement and engagement on all levels of the call process (i.e.: call topic definition/eligibility issues for PAOs participation and/or funding/dissemination/evaluation/PPIE-oriented monitoring indicators), but also engagement in research project design. It will also focus on ERDERA calls dissemination and promotion to PAOs, support to PAO willing to participate to research projects by providing additional information and answering specific requests. Finally, this group will drive a joined-up thinking with PPIE group about the place of PAOs as funders of European research projects, especially for JTCs. In addition, the group may serve as an advisor for PAOs willing to fund RD research (providing guidelines and advice) as well as proposing innovative ways of funding research with side funding from EU PAOs (federations or disease-specific). **In Year 1**, the working group will be established and a call for interest launched among European PAOs to benefit from their experience as research project partners and/or funders, especially from underrepresented countries (not limited to EJP RD or ERDERA beneficiaries). This call will be disseminated by EURORDIS channels as well as through ERDERA and partners channels. The outcome of this call for interest will be the organisation of a workshop aiming at mapping the efforts of PAOs in RD research as well as paving the way for further interaction and synergies with the ERDERA funding research schemes. The link

with the PPIE group (WP1) will be established to take stock of funding opportunities of JTCs by the PAOs. The group will be closely involved in the first and second ERDERA JTC call topic definition as well as in the preparation of the launch of the calls (ST3.1.1, ST3.2.1.1). The group will raise awareness among JTC national contact points of the need to include PAOs in each consortium and will act as the focal point to answer all queries from PAOs related to an ERDERA research call.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**4**		**Start Date or Starting Event**		**M1: September 2024**	
Set of Activities Title	**Clinical trial call management**					
Short name of participants & (No)	FTELE (5)	DLR (3)	WDO (120)	QUB-UK* (172)	HRB** (67)	
Person Months	1.6	1	1	0.6		
Start month	M1		**End month**		M12	

** *Beneficiary providing in-kind contribution*

State of the art behind this WP

There are around 6200 rare diseases (RD), 70% of which are genetic in origin1. Collectively, up to 36 million people in Europe are living with a rare disease2. Therefore, RDs are a major public health issue requiring effective interventions to be identified to ease this burden on patients, friends and families, society and health systems. Many RDs have an early or very early onset and/or lead to a significant decrease in life expectancy. Most of them cause chronic illnesses that heavily affect affected persons' quality of life and negatively impact on the health care system. and health care system. and even more evident during and since the COVID-19 pandemic and at times of disasters e.g., earthquakes and war. Current treatments are usually supportive rather than disease-modifying, leaving most patients with rare diseases with considerable unmet medical needs. Tackling these issues will require valid and reproducible clinical trials, and opportunities for those affected by rare diseases to influence and participate in these trials. However, conducting clinical trials in rare diseases presents unique challenges. Considering that 85% of RD affect < 1/1,000,000 people, the cohorts are often very small.

Methodology

The call topic selection and design will be in line with the processes described and in close collaboration with WP 3, T3.1 and will illustrate the goal of the initiative, the eligibility criteria (for applicants and institutions/centres) and relevance requirements, as well as the different phases of the evaluation process. In close collaboration with WP24 ERDERA will promote the inclusion of centres from underrepresented countries in clinical trials. Additionally, policies related to data and results exploitation, compliance with clinical and regulatory standards, industry involvement and public and patient engagement will be described in the call text. The call text would be discussed and approved at the Board of Funders (BoF) and Governing Board (GB) of the Partnership. Based on the experience of the RD partners and on previous EJPRD calls, the evaluation process will have 3 main phases (see T2.0 for further details):

- Pre-proposal submission and triage phase (through peer review): the evaluation will focus on the scientific merit and relevance/significance of the clinical research proposal, and it will be conducted by clinical trial scientific committee (CTSC).

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- Evaluation of selected full proposals (through peer review): the evaluation will focus on the robustness and feasibility of the clinical protocol, and it will be conducted by the clinical trial evaluation board (CTEB).
- Selection of excellent projects and funding by milestones.

Both the CTSC and CTEB will ensure to have a geographical and gender balanced composition. This methodology will ensure that only relevant proposals will receive further support (Regulatory/CT management/statistical support will be provided to applicants who pass the first step of evaluation; Please see T4.2 for further details) and proceed along the evaluation process. It will require the design of the trial and its conduct to consider specific requirements and clear milestones, which would increase chances of success and allow best use of the resources. FTELE has extensive expertise in call design opening and management; currently managing many competitive extramural initiatives and two intramural non-competitive programs. FTELE conducts a peer review process which is quality certified.

A multistep application is time saving for researchers (burden of initial application is reduced) and it allows for feedback and a better overall project design. Indeed, the quality of full applications should be improved, aligning with the idea to accelerate the development of a robust and meaningful trial that would eventually lead to a treatment.

The 3 tasks will be carefully planned and will rely on the expertise and previous experience of RD partners. The interaction with the CRN and the Accelerator Hub will be an added value, for both project implementation and results exploitation, eventually.

Objectives

T4.1. will be the only WP4 task with planned activity on the Year 1. The objectives of this T4.1 – Development of the call framework are:

- Topic selection and definition of eligibility criteria.
- Preparation of the call and establishment of the joint call secretariat.
- Platform implementation.

Description of Programmed Activities

T4.1. **Develop the call framework (M1-M12)** *TL: FTELE, DLR, WDO, QUB-UK; Contributors: HRB.*

The following task is planned during Year 1. T4.1. aligns with GO:2; SO:3; OO:1,5.

- The selection process for the topic of the call will be centralised and will be done according to the same procedure adopted in close collaboration with WP3. FTELE, DLR, WDO, and QUB-UK and HRB will draft the text of the call by M12, and finalize it by M18, as well as the timing for proposal submission, in close collaboration with the Board of Funders which will also give final approval. A second call will be opened at M36. Specifically, this will be an open competitive call, open to researchers, clinical centres and patient organizations from all Horizon Europe eligible countries. The call text will clarify the eligibility criteria: the type of clinical trial (e.g., phase (I/II) and intervention – drug/medical device/ other), topic (e.g., first-in-indication, next-in-class, etc) and status of the intervention (e.g., proprietary products, off-patent products, ODD, etc). A minimum of recruiting centres and/or countries will be specified, and the number and role of each centre and partner will need to be defined in the application. The potential roles for companies will be specified and guidelines about their involvement (at each stage of the call and of the project) will be provided. Additionally, the call text will have to contain information about the minimum requirements for the clinical trial (e.g., GCP, ethical approvals, etc), funding management (a central funding agency, y) and the proven and meaningful involvement and contribution of patients, Patient Associations, patients' representatives, patient experts and the public in the design and implementation of the project. Specific attention will be given to data sharing, the return of the data back to the

patient, the publication of positive and negative results in open access journals etc. TLs will also identify the time frame of the call (opening, closure, peer review, final decision etc). To avoid conflicts of interest, a strict firewall between the parties deciding on call topics and partnership beneficiaries will be established (see WP3).

- The design of the call will be based on the model under development by ERA4Health to demonstrate the feasibility of the funding model. The MAB or specific thematic groups that could stem from it will be involved in the discussion. The ultimate goal is to develop a funding model that overcomes bottlenecks encountered under JTC2016 E-Rare-3 and fund multinational RD CTs. In addition, ERDERA will contribute via ECRIN to the Accelerating Clinical Trials in the EU (ACT EU) initiative to integrate their recommendations for multinational CTs in the call text of the ERDERAs' calls. The final call documents will be presented to the Board of Funders for their approval. The TL will be responsible for drafting all necessary documents including Memorandum of Understanding, Call text, Governance and evaluation procedures, Guidelines for applicants, Proposal templates and other documents that might become relevant. In addition, the TL will set up the CT call secretariat, which will act as central support to the applicants regarding all aspects of proposal drafting and submission.
- Implementation of the call on the platform and testing.

T4.2. Open the call and select trials for funding (starts M19) *TL: FTELE; Contributor: WDO*. T4.2. aligns with GO:2; SO:3,4; OO:1,4,5.
FTELE with the contribution of WDO will open the first call in the second half of Year 2. The second call will not be open before Year 4. **There are no planned activities for this task during Year 1.**

T4.3. Project implementation, project monitoring, and financial management (starts M38) *TL: FTELE; Contributors: IT-MOH; CSO-MOH, WDO*. T4.3. aligns with GO:2; SO:1; OO:1,5.
The objectives of this task are to ensure a smooth implementation of the funded trials and to follow the achievement of project specific milestones for each funded clinical trial. Indeed, for each project, funding will be paid in instalments, which will be triggered by the achievement of specific milestones. This is therefore a crucial task to ensure an efficient use of resources. **There are no planned activities for this task during Year 1.**

Additional deliverables *(additional to those included in part B of the proposal)*

Other documents related to CT call text and procedures.

Set of Activities Number	**5**		**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Networking to share knowledge on research**						
Short name of participant & (No)	LMT (6)	ZonMw (7)	FFRD (29)	ANR (4)	EURORDIS (26)	WDO (120)	GA UK* (168)
Person Months	1.25	2.00	0.50	0.40	0.20	0.20	0.20
Short name of participant & (No)	CSO-MOH (49)	FGB (23)					
Person Months	0.20	0.50					
Start month	M1		**End month**		M12		
**Associated partners providing in-kind contribution*							
State of the art behind this WP							

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Networking between stakeholders is essential to understand and translate the needs of the persons living with a rare disease (PLWRD) into diagnostics, (new) therapies and to understand the impact of these diseases on the life of patients, families, and their surroundings, including friends, school and work environments. In the EJP RD, the Networking Support Scheme (NSS) to share research knowledge on RDs and rare cancers was established to support the organisation of face-to-face or hybrid meeting (conferences. workshops). This competitive funding scheme, even if small, was very much appreciated by many stakeholders, and especially patient advocacy organisations. This funding scheme will be continued in the ERDERA to empower PLWRD to be full partners in RDs research, to involve stakeholders from widening countries1 in new or expanding research networks and to get and keep young researchers engaged in RDs research. The NSS will also target to support the building of new research networks for underserved RDs or cohorts of undiagnosed patients that are suspected of living with a RD.

The networking support scheme will encourage applicants to apply to other funding schemes, in ERDERA (e.g., in Joint Transnational Calls (WP3) or in Clinical Trials (WP4), in EC Calls (e.g., Marie Sklodowska-Curie Actions or COST actions) or in R&I calls like in Innovative Health Initiative or support the building of global multinational research networks (WP25).

The exchange of knowledge facilitated through this networking support scheme will also lead to an increased uptake of research results by providing the space to share diagnostic practices and guidelines and strengthen the collaborations with other national (WP23, WP24) or international stakeholders (WP25).

Methodology

The Networking Support Scheme will support the organisation of conferences, workshops, or stakeholders' meetings. It will be continuously open after the launch of the Call. The applications for this funding scheme will be collected twice a year and the application will be evaluated by external reviewers (researchers/clinicians/representatives of patient advocacy organisations) in a competitive way using the evaluation criteria from the EC. The Networking events will be funded by EC budget.

Networks of researchers/clinicians and representatives of RD support groups and patient organizations from countries involved in the ERDERA will be eligible to apply. The consortia should include beneficiaries from at least three different eligible countries at the time of application. Additional beneficiaries from countries not involved in the ERDERA may be also part of the consortium, depending on the scope of the networking event. However, they will not be eligible to directly receive funds (i.e., to be a grant holder). There will be no limitation on the size of a network. Nonetheless, the maximum grant amount will be limited to 30 000 € for each funded networking event.

Objectives

The main objective of this WP is to encourage sharing knowledge on research among relevant transnational and transcontinental RD stakeholders including clinicians, basic researchers, patients' organisations/RD support groups, as well as PhD students, post-docs, other early career researchers and industry through funding of networking events. These events will support building of new transnational and/or transcontinental research networks or expanding existing research networks on RDs and rare cancers and will support patient-need led research, and inclusion of stakeholders of widening countries and young researchers. **The specific objectives of this WP for Year 1 are**:

- The experience and lessons learned from the scheme to fund networking events, developed in the EJP RD, will be implemented in Call documents and in evaluation procedure.
- The Call will be launched for interested applicants in Year 1.
- A helpdesk for this funding scheme will be installed for interested applicants and potential evaluators.

Description of Programmed Activities

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

T5.1. Preparation and launching of the funding scheme (M1-M9) *TL: LMT, ZonMw; Contributors: FFRD, ANR, EURORDIS, WDO, GA UK, CSO-MOH, FGB.* T5.1. aligns with GO:1-3; SO:3-5; OO:1,4,5.
T5.1.'s objective is to prepare the Call documents, application and evaluation procedures of the funding scheme to fund networking events. A Working group will be set up to prepare the documents for the application and evaluation procedure of the Networking Support Scheme. This Working group will be composed of the TLs and contributors.
The experience and lessons learned of the Networking Support Scheme in the EJP RD will be used to implement the support for networking at European transnational and transcontinental level. Financial support will be provided for the organisation of conferences or workshops to foster networking of RD and rare cancer stakeholders to (list is not exhaustive and will be finalised with the Working group):

- Share existing knowledge on a specific (group of) RD(s) or rare cancer(s) or on cohorts of undiagnosed patients that are suspected of suffering from a RD(s);
- Improve the knowledge on RD(s), especially for the underserved RDs and rare cancers;
- Encourage further innovation and research, e.g., by preparing an application for another networking grant or training grant (e.g., for COST Actions, Marie Skłodowska-Curie Actions, etc.), research grant or clinical trial grant in ERDERA (WP3 and WP4), or in other EC or international programmes;
- Share knowledge and best practices on data sharing and /or novel/validated methodological approaches for clinical research;
- Encourage involvement of stakeholders from widening countries;
- Encourage involvement of young researchers and clinicians.

It is expected that networks of researchers/clinicians and patient organizations from countries involved in the ERDERA may be eligible to apply. The consortia should include beneficiaries from at least three different eligible countries at the time of application. Additional partners, from countries not involved in the ERDERA, may be also part of the consortium, depending on the scope of the networking event. However, they will not be eligible to directly receive funds. There will be no limitation in the number of participants. Nonetheless, the maximum grant amount will be limited to 30 000 € for each funded networking event. The applications will be selected through competitive calls.

The Call documents that have to be prepared are e.g., public documents, including the Call text and application form. Furthermore, criteria for evaluation of applications by an Evaluation Committee will be established, a pool of evaluators will be prepared that will be composed of clinicians, researchers and patients/patient representatives, confidential guidelines for the Evaluation Committee will be written and webinars for applicants and tutorials for evaluators will be prepared. The documents will be submitted for validation of the EC before opening of the call. The Call will be published widely through the same channels as the Joint Transnational Calls (WP3) with help of WP Communication (WP2) and launched at Month 9. The webinars for the applicants will be published on the ERDERA website (WP2).

The Call will be continuously open after its launch. The applications for this support scheme will be collected twice a year and the applications will be evaluated by the Evaluation Committee in a competitive way. The first collection date will be in early Year 2.

T5.2. Evaluation of the selected proposals after each collection date (M9-M12) *TL: LMT, ZonMw; Contributor: FGB.* T5.2. aligns with GO:1-3; SO:3-5; OO:1,4,5.
The Call will be open from M9, and the first collection date will be in early Year 2. Therefore, ST5.2. on evaluation of the proposals will start in ERDERA Year 2 and will be continued throughout the duration of the project.

T5.3 Quality management (M9-M12) *TL: LMT, ZonMw; Contributors: FFRD, ANR, EURORDIS, WDO, GA UK, CSO-MOH, FGB.* T5.3. aligns with GO:1-3; SO:3-5; OO:1,4,5.

T5.3 starts at Year 1 and will be continued throughout the duration of the project. The specific objective of the ST is to ensure the quality of the implementation of the funding instrument: monitoring of the administrative, evaluation, funding processes to improve them along the duration of the funding scheme. **In Year 1**, a specific helpdesk will be set up to answer the questions of applicants and of (potential) evaluators after the launch of the Call. This helpdesk will e.g., support less experienced applicants in the administrative procedures to submit the application.
Additional deliverables *(additional to those included in part B of the proposal)*
None

Set of Activities Number	**6**		**Start Date or Starting Event**		**M1: September 2024**	
Set of Activities Title	**Diagnostic Data Availability**					
Short name of participant & (No)	UT (8)	CNAG (10)	UTARTU (9)	UMCG (19)	CRG-CERCA (145)	CAD (1.1)	RS (65)
Person Months	27	24	15	9.6	5	2	2
Short name of participant & (No)	CENTOGENE (43)	INSERM_IT-GGB (1)	CCRI GmbH (42)	VIB (147)	UGENT (118)	KU Leuven (77)	MUS (80)
Person Months	2.4	40	3	3	3	3	3
Short name of participant & (No)	UoC (117)	MUH (81)	Aarhus UH (133)	REGIONSYD (87)	REGIONH (48)	INSERM_U974 (1)	UO (149)
Person Months	3	3	3	6	3	3	3
Short name of participant & (No)	APHP (24)	INSERM_U1112 (1)	CHU Dijon (46)	TUM (12)	NKUA (84)	RCSI (95)	UNICAMPANIA (116)
Person Months	3	3	3	3	3	3	3
Short name of participant & (No)	OPBG (88)	AOU Meyer IRCCS (38)	UNISI (143)	REUH (93)	VULSK (27)	SRUMC (11)	LUMC (16)
Person Months	3	3	3	3	3	3	3
Short name of	Erasmus MC (53)	IGC PAN (71)	UKCL (119)	CIBER (125)	IBG (68)	UCAM* (174)	UNEW*(169)

participant & (No)							
Person Months	3	3	3	3	3	3	3
Short name of participant & (No)	UCL* (173)	Aalborg UH (130)	UANTWERPEN (128)	IPG (148)			
Person Months	3	3	3	3			
Start month	M1			**End month**	M12		

State of the art behind this WP

Diagnosis has critical value for RD research, clinical practice and PLWRD. Diagnosis of novel or established RD enables research and knowledge (i) on function of genes, on non-coding genome elements and pathogenic variants, (ii) on patho-mechanisms of RD leading to the development of innovative therapies (WP11,12), biomarkers and outcomes (WP9,10). Only exact diagnosis enables engagement of RD patients and their data to clinical trials, natural course studies and biomedical research. Finally, in clinical practice diagnosis is key for an informed disease management, has social consequences (e.g., family plans, access to social services/ education/ disability levels) and enables engagement in patient organisations.

However, despite improvements in diagnostics and research possibilities for RDs, time to diagnosis is on average still years long and a large number of people with a suspected RD remain without a molecularly proven diagnosis. In healthcare systems, where exome sequencing or genome sequencing are becoming standard of care, the diagnostic yield varies between 20-70% depending on the type of RD, inclusion criteria, sequencing strategy, and analysis standards.

In recent years, various international initiatives and EU projects, including GA4GH, IRDIRC, 1+MG, EJP-RD, and the ELIXIR RD-Community, have worked towards providing foundational (e.g., data standards, infrastructure) resources for RD research diagnostics based on (re-)use of genomic as well phenotypic and clinical data across Europe. In 2018, the EU project Solve-RD – Solving the unsolved[1] – was initiated and for the first time succeeded in building a Pan-European ERN based expert and data-secure sharing and research analysis ecosystem. Building upon existing tools and resources such as the RD-Connect GPAP[2] and the EGA[3] and international standards such as provided by GA4GH[4] as well as RD standards and ethical policies from EJP RD[5], this collaborative infrastructure enabled the sharing and systematic (re)analysis of over 22,000 REAL (RE-Analysis Logistics: genomic raw data, standardised phenotypic and pedigree information, meta-data) datasets across Europe.

Methodology

The primary objective of WP6 is to build upon the accomplishments of Solve-RD, EJP-RD and ERNs as well as the infrastructural elements being built by Genomic Data Infrastructure (GDI) project (start in 2022) and 1+MG to deliver diagnostic research data availability on a European scale so that data research re-analysis methodologies can be applied for solving unsolved RD patients, to shorten time to diagnosis and enable the development of new therapies and treatments (WP11 and 12) as well as biomarkers and outcomes (WP9,10).

To this end, the CRN diagnostic research workstream will build on the existing ERN ecosystem and it will also include national undiagnosed RD programs (UDP) as well as national diagnostic centres and programs. This way, both scaling up the proven collaborative Solve-RD infrastructure that has been using a distributed data analysis approach and implementing a federated approach that is based on

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national 1+MG/GDI infrastructural elements - designing, building and testing the GDI infrastructure that will enable access to genomic data in Europe started in 2022 - will be feasible. This approach will allow to deliver on GO1 as well as to develop, test and scale-up the federated approach using early adopters (e.g. CAD (France), GMS-RS (Sweden)) from the beginning of the project.

The work of WP6 will be closely coordinated with the Data Services Hub, particularly using the services provided by WP14 (Data readiness for federated approach) and WP15 (Data analysis services). WP6 will also prioritise unwavering compliance with ethical considerations, ensuring responsible and ethical data usage throughout the project.

To ensure the quality and integrity of the data included in the project and monitor the data sharing, a Data Availability Committee will be established from the project's inception. This committee will consist of representatives from WP6, WP7, and WP8 from the CRN Diagnostic research workstream and WP15 from the Data Hub workstream. Leveraging the Solve-RD data infrastructure and its associated policies (data sharing, data access, publication, Code of Conduct; WP6 will up-scale and consolidate a secure environment for ERNs, UDNs and diagnostic centres to share data on undiagnosed RD patients. More than 60 diagnostic centres and programmes (representing more than 12 ERNs, 22 countries) have already stated their interest to be involved in the work of the ERDERA diagnostic research workstream amounting to a putative availability of a large number of datasets (>150.000) during the first three years of ERDERA.

Notably, a network of diagnostic research centres situated in the underrepresented countries will be established to ensure access to and impact of the diagnostic research workstream in these countries. It will consist of all centres contributing to the diagnostic research workstream, be led by UTARTU, MUH and University Hospital Vilnius. The network will particularly focus on facilitating the access to the diagnostic research workstream in these countries but also tailor the WP6 and WP7 activities to the specific needs of these countries.
WP6 in coordination with WP7 will apply a phasing approach: **Year 1-3:** re-analysis approach focusing on exome and genome data using a distributed approach and early adopters of a federated approach; Year 4-7: re-analysis approach including long read sequencing data mainly using a federated approach based on national 1+MG/GDI infrastructures.

To monitor and oversee sample and omics metadata collation, available cohorts, datasets, and data types as well as conducted analysis and returning research results (most importantly newly diagnostic patients), a dedicated CRN diagnostic research data management system will be implemented (T6.1 and T6.3). This data management system will be developed in WP15 following WP6 recommendations and will build on the Solve-RD RD3 solution, the GPAP and its cohort module[6]. T6.3 will apply this data management system for returning results to data providers in a timely manner. The CRN Diagnostic Research data management system will allow to monitor how time-to-diagnosis will be shortened in the real-life (diagnostic) setting.

Objectives

The objectives of Year 1 are the following:

- Instigate the establishment of the CRN diagnostic data availability and collation effort that comprises ERNs, national UDPs and national diagnostic centres so that 10,000 data sets can be shared during the first 12 months.
- Instigate the implementation of data standardisation, sharing, federation and quality control so that data analysis methodologies can be applied.
- Set up the processes to be able to access and federate the data during the project to enable the re-analysis of large datasets and return research results to the clinics, to RD patients and their families.

Description of Programmed Activities

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T6.1. Coordinate and consolidate the diagnostic research data availability and collation effort in the diagnostic research workstream (M1-M12) *TL: UT, CNAG, UTARTU. Contributors: CRG-CERCA, UMCG, CIBER, ISCIII, Aalborg UH, AarhusUH, AOU Meyer IRCCS, APHP, CCRI GmbH, CHU Dijon, Erasmus MC, IBG, IGC PAN, INSERM_IT-GGB, INSERM_U1112, INSERM_U974, MUS, RCSI, REGIONSYD, UCAM, UNEW, UKCL, UNICAMPANIA, UNISI, UoC, VIB, VULSK, UO, ERN HCPs, diagnostic centres and RD NMGs throughout Europe linked to ERNs and UDPs*. T6.1. aligns with GO:1; SO:2,5; OO:3,5.

DATA AVAILABILITY COMMITTEE: Data Availability Committee will be established to coordinate data availability activities, encompassing both distributed and federated approaches. This committee will comprise delegates from WP6, WP7, and WP8 from the CRN Diagnostic Research workstream and WP14 and WP15 from the Data Hub workstream. Expertise will be organised in several working groups and monthly calls will be planned during Year 1 to ensure outcomes delivery:

- **Infrastructure working group:** The WG will prioritise IT requirements and needs, focusing on the transition from a distributed re-analysis model to a federated approach across the diagnostics research workstream (WP6, WP7 and WP8), and align with GDI/1+MG and to IT/Data Hub/streams, in particular WP15. **Outcome Year 1:** list of prioritised IT requirements and needs distributed to all involved parties.
- **Data policies working group:** The WG will update, adapt and consolidate data policies and agreements (data sharing within and outside consortium, data federation policies, code of conduct, data protection impact assessment, publications, etc.). **Outcome Year 1:** data policies approved and published in the project website.
- **Standards and quality working group:** The WG will update, adapt and consolidate standards, minimum quality criteria and processes for omics, phenotypic and meta-data collation and submission. This WG will align with international standards and recommendations such as the ones from GA4GH and the GDI project for genomics interoperability. **Outcome Year 1:** standards to be used and thresholds on minimum quality criteria established for all type of omics data and phenotypic information to be submitted.
- **Federated working group:** a working group including diverse stakeholders engaged in the creation of an EU RD federated model will be established, which will include participants from the 1+MG RD use case, GDI, ERNs and diagnostic centres and the ERDERA Data Services Hub. **During Year 1,** a workshop will be conducted with 1+MG and GDI delegates to align, prepare, pilot and scale-up towards the federated re-analysis approach through the development of interconnected CRN Diagnostic Research satellite ecosystems based on development status of national 1+MG/GDI infrastructure. In collaboration with WP20, different types of training activities (workshops, train the trainer, webinars, etc) will be planned for the following years to transfer this federated capacity building into national nodes. France and Sweden have already expressed their interest in joining the CRN Diagnostic Research ecosystem adopting a federated model and will be approached to be involved as early adopters. **Outcome Year 1:** roadmap for implementing the federated approach within the CRN Diagnostic Research Workstream.

CENTERS ONBOARDING: Based on the interest received (> 50 diagnostic centres and programmes from 22 countries) submissions will be prioritised for phase 1 (**Year 1–3**: exome and genome data) according to centres data availability status, type of contribution (distributed or federated model) as well as ethical and legal basis for data sharing. **During Year 1**, focus will be on data collation from the distributed approach and early adopters of the federated approach in alignment with the outcomes from the federated WG. Additional centres will be contacted together with initiatives across and beyond EU to join the project as data submitters or collaborate with a federated discovery model. Outcome M3: Prioritised list of data submitters centres based on interest received to start data collation at M4. **Outcome Year 1:** Updated prioritisation list for Year 1 to 3, including new submitting centres and/or federated nodes.

UNDERREPRESENTED COUNTRIES ONBOARDING: To ensure underrepresented countries are well represented, all centres willing to participate in ERDERA will be informed and supported by establishing a network of diagnostic research centres in underrepresented countries. This network will be a central actor of the ERDERA diagnostic research workstream, and based on NMGs (WP23),

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ERNs (affiliated partners and full members from underrepresented countries) and interaction with Joint Action JARDIN that includes all EU countries and 1+ MG. Monthly meetings will be established to gather centres needs and concerns that will be transmitted to the Data Availability Committee. **Outcome Year 1:** Underrepresented countries network established and periodic communications ongoing.
DATA MANAGEMENT SYSTEM: A data management system based on the RD3 platform used in Solve-RD will be implemented in collaboration with ERDERA WP15. Preliminary work will be done towards identifying missing needs and requirements to ensure all information is available in this central database and compatible with a federated approach. Special focus will be made to ensure proper metadata collection of the different types of omics, tracking of results generated within the project by WP7 and WP8 and ensuring feedback from the data interpretation task forces implemented in WP7 is included to enable tracking of newly diagnosed patients for returning of results to national centres in T6.3. **Outcome Year 1:** Requirements and needs of the CRN Diagnostic Research workstream to be developed in Data Management System have been identified and reported to WP15.

T6.2. Data standardisation, sharing, and federation (M1-M12) *TL: CNAG, UTARTU, CAD. Contributors: UT, CRG-CERCA, UMCG, RS, GMS-RS, NKUA, UANTWERPEN, IPG,UO, Aalborg UH, Aarhus UH, AOU Meyer IRCCS, APHP, CCRI GmbH, CHU Dijon, Erasmus MC, IBG, IGC PAN, INSERM_IT-GGB, INSERM_U1112, INSERM_U974, MUS, RCSI, REGIONSYD, UCAM, UNEW, UKCL, UNICAMPANIA, UNISI, UoC, VIB, VULSK, UO ERN HCPs, diagnostic centres throughout Europe linked to ERNs, RD NMGs and UDPs.* T6.2. aligns with GO:1; SO:2,5; OO:2.
COLLATION OF THE FIRST 10,000 REAL DATASETS: Based on the centres prioritisation defined and in alignment with the standards agreed in T6.1, pheno-clinical information together with its corresponding omics metadata and files will be collated, mostly exome and genome data in Year 1. Data entry point for genomic and phenotypic information in Year 1 will be consolidate through the RD-Connect GPAP and distributed to the different data hubs for downstream analysis and/or provided by the implementation of a federated approach (see T6.1), linking ERDERA CRN satellite ecosystems. We will collaborate with ERDERA to help data submitters that might not have clinical data in a standardise format to access clinical data readiness services developed within T14.1. **Outcome Year 1:** 10,000 harmonised datasets from the distributed and/or federated approach are available in the CRN Diagnostic Research Ecosystem.
METADATA CENTRAL REPOSITORY: To ensure all clinical information and metadata submitted through the RD-Connect GPAP or satellite federated systems is linked/transferred to the CRN data management system for coordination and partners to access and T6.3 to track files distribution and results. **In Year 1,** a similar instance of the Solve-RD RD3 data management system, meaning that some of the required fields and needs identified in T6.1 might not be available when the first datasets will be submitted/ federated, and information will be completed retrospectively if needed. **Outcome Year 1:** All metadata and clinical information collated and possible to be stored in the CRN Diagnostic Research Data Management System is available for the first 10,000 datasets.
DATA QUALITY CONTROL: Based on the data quality requirements established in T6.1, identify automated data quality control checkpoints for each type of data including phenotypic information, genomic information and other omics data. For example, for phenotypic information, if a minimum set of HPOs is requested, the system will enable identification of cases with less terms. Same would apply for minimum depth of coverage for exomes and genomes, etc. For datasets that do not pass a specific threshold, the CRN diagnostic research submission helpdesk will inform submitters and a decision on how to best proceed will be taken in agreement.
SUBMISSION SUPPORT: A "submission toolkit" including guidelines about standards and quality threshold established in T6.1, and short videos on how to submit clinical information and different types of omics metadata and files will be created and distributed among all data submitters. A dedicated CRN diagnostic research submission helpdesk to help resolving data submitters issues and doubts will be created involving members from all resource submission parties.

T6.3. Data access and returning research results (M1-M12) *TL: UT. Contributors: CNAG, CRG-CERCA, UMCG, CAD, RS, GMS-RS, NKUA, UANTWERPEN, CENTOGENE, IPG, UO, Aalborg UH,*

Aarhus UH, AOU Meyer IRCCS, APHP, CCRI GmbH, CHU Dijon, Erasmus MC, IBG, IGC PAN, INSERM_IT-GGB, INSERM_U1112, INSERM_U974, MUS, RCSI, REGIONSYD, UCAM, UNEW, UKCL, UNICAMPANIA, UNISI, UoC, VIB, VULSK, UO, ERN HCPs, diagnostic centres throughout Europe linked to ERNs and UDPs, RD NMGs. T6.3. aligns with GO:1; SO:2,5; OO:2.

DEFINITION OF THE TYPE OF DATA TO BE AVAILABLE Engage with the CRN data analysis hubs and ERDERA RD stakeholders, including researchers, clinicians, and patient advocacy groups, to gather input on which type of data is needed to be accessible for re-analysis, including analysis results. This work will be done in alignment with suitable GDI recommendations. **Outcome Year 1**: List of data types recommended to be made available to the RD Community.

DATA DISTRIBUTION ACROSS THE CRN DIAGNOSTIC RESEARCH ECOSYSTEM: The European Genome-Phenome Archive (EGA) infrastructure will be linked to the CRN Diagnostic Research ecosystem and established as the central data repository for the distributed approach, guaranteeing data distribution and sustainability throughout the ERDERA project. The 10,000 REAL datasets collected in T6.2 during **Year 1** of the distributed approach will be made accessible for distributed analysis in WP7 and WP8 data hubs. To ensure GDPR compliance and prevent data from leaving Europe, the EGA Spanish node located in Barcelona will be used, creating a secure and compliant environment for data handling in ERDERA. **Outcome Year 1**: data from the first 10,000 datasets collated through the distributed approach is made available to data hubs.

RETURNING OF RESEARCH RESULTS: Together with WP7 and WP8 and in alignment with GA4GH policy recommendations, a comprehensive results workflow will be established to ensure diagnostic findings from the CRN Diagnostic Research ecosystem are returned to national centres. This process will facilitate the subsequent dissemination of information to patients and their families. **Outcome Year 1:** meeting with all involved stakeholders to define a results-return workflow and identify needs and requirements to be implemented.

Additional deliverables *(additional to those included in part B of the proposal)*

Deliverables related to T6.1:

- Report on Data Availability Committee establishment and organigram (M6)
- List of standards and minimum quality criteria for data submission (M6)
- List of prioritised submitting centres, including early adopters of the federated approach (M12)
- Identification of additional requirements and needs of the CRN Diagnostic Research workstream to be developed in Data Management System (M3)

Deliverables related to T6.2:

- 10,000 harmonised datasets from centralised and/or federated approaches available in the CRN Diagnostic Research Ecosystem (M12)
- Data collation toolkit (M3)

Deliverables related to T6.3:

- List of data types recommended to be made available to the RD Community (M6)
- Report on results return workflow to national centres and beneficiaries (M12)

Set of Activities Number	**7**		**Start Date or Starting Event**			**M1: September 2024**	
Set of Activities Title	**Genome re-analysis research pipeline**						
Short name of participant & (No)	CNAG (10)	SRUMC (11)	UT (8)	CAD (1.1)	UU (121)	CENTOGENE (43)	ISCIII (72)

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Person Months	27	33	18.0	6.0	6.0	3.6	6.0
Short name of participant& (No)	KU Leuven (77)		INSERM_U974 (1)		UNEW*(169)		CHEO-RI* (152)
Person Months	1.2		1.2		6.0		
Start month	M1			**End month**		M12	

**Associated partners providing in-kind contribution*

State of the art behind this WP

Despite improvements in diagnostics and research possibilities for RDs, now providing access to exome and genome sequencing, the genetic basis for 33% (3,032 of 9,321, OMIM accessed 18-08-203) of suspected Mendelian RD remains elusive. In healthcare systems, where exome sequencing or genome sequencing are becoming standard of care, the diagnostic yield varies between 20-70% depending on the type of RD, inclusion criteria, sequencing strategy, and analysis standards [1,2], leaving many patients without a diagnosis. Although it has been shown that genomic data re-analysis alone can increase the diagnostic yield, in absence of guidelines on reanalysis strategies, it is not routinely undertaken due to the time and multidisciplinary expertise required, and associated costs. However, the EU project Solve-RD has recently shown that an ERN-focussed and cost-efficient state-of-the-art, comprehensive, and systematic re-analysis effort of exome and genome data increased expertise levels, yielding >12% of novel diagnoses, based on newly described disease genes, as well as improvements in identification, annotation, and interpretation of genomic variants. In more detail, bioinformatic experts from participating RD centres joined themselves into Data Analysis Task Forces (DATF) which, organised in Working Groups, implemented state-of-the-art and innovative methods to call and annotate all types of variants (SNV/InDels, including dedicated mtDNA analysis and non-canonical splice sites, CNVs, STRs, MEIs and SVs in general), providing a uniform and systematic analytical framework for all individuals with a RD. The analysis was fuelled by a distributed infrastructure, including the RD-Connect GPAP (data ingestion, SNV/InDel calling and a user-friendly interface), three HPC clusters (for amongst others, SV calling, and de-novo mutation analysis), a Cloud infrastructure (for specific analyses conducted by non-EU partners as well as data storage and sharing) and the EGA (for data transfer/sharing between partners). A database called RD3 enabled tracking the data within the infrastructure. The molecular and clinical expertise available across the ERN were joined within ERN-specific Data Interpretation Task Forces (DITF). The DITFs systematically prioritized the variants through exchange of expertise and up-to-date knowledge to identify new diagnoses, which they reported back to the patients through the referring HCP. With this structure, Solve-RD has provided the largest pan-European genome research re-analysis effort to date, including data from 6 ERNs and 1 UDP (EURO-NMD, ERN GENTURIS, ERN ITHACA, ERN-RND, ERN EpiCARE, ERN RITA, and UDP-Spain).

Although this approach has worked well, 18 other ERNs have not yet benefitted from the complementary expertise levels available across ERNs, nor have other UDPs or national RD diagnostic centres. Moreover, it is necessary to move towards a federated system to enable the participation of centres which cannot submit to a distributed infrastructure, but also for scalability and sustainability reasons. The latter would also allow for a more extensive collaboration with other international large-scale RD initiatives (e.g. Care4Rare Solve, UDN-Australia, US UDN, UDN-I, Genomics England, DECIPHER, Japan) thereby addressing IRDiRC's Goal 1 that all currently undiagnosable individuals enter a globally coordinated diagnostic and research pipeline for continuous reanalysis and access to the most innovative data strategies. Although it is necessary to move as fast as possible from a distributed data re-analysis model to a federated one, there are several challenges that will require close multidisciplinary collaboration and innovation. The Genomic Data Infrastructure (GDI) project "is enabling access to genomic and related phenotypic and clinical data across Europe. It is doing this by

establishing a federated, sustainable, and secure infrastructure to access the data. It builds on the outputs of the Beyond 1 Million Genomes (B1MG) project and is realising the ambition of the 1+Million Genomes (1+MG) initiative". However, although 1+MG has a Working Group on RDs and B1MG did the Proof on Concept on RDs, GDI does not include a use case on RDs, and specially not on data re-analysis. Therefore, WP7, in collaboration with the whole CRN Research Diagnostics Stream and the Data Services Hub, aims to contribute to the design, planning and implementation of the federated re-analysis use case in coordination with 1+MG/GDI, clinical partners and data scientists.

Methodology

WP7 will coordinate and apply a genomics diagnostic research pipeline, aiming to move from a distributed infrastructure to a federated infrastructure within European, and with similar efforts internationally (United Kingdom, Canada, Australia). Clinical and molecular geneticists' expertise will be organised in super-DITFs (Data Interpretation Task Forces), set up according to similarity of disease groups and number of available datasets. Bioinformatics expertise will be organised in a single DATF (Data Analysis Task Force) with several Working Groups (WGs). Coordination within groups will happen in monthly online meetings, and between group coordination will happen in a bi-monthly online meeting between all the groups. 'Data challenges' for WGs will be organised yearly to allow for continuous evaluation and evolution of the pipelines, whereas 'Solvathons' coordinated by the DITFs will be held annually to engage all HCP submitters in finding novel diagnoses and providing hands-on experience in interpretation of novel data sets. This DITFs-DATF structure will allow a patient(/family)-centred clinical research evaluation. Moreover, this evaluation will move beyond the coding sequence, and will include the evaluation of potential disease-causing variants in the non-coding space, through global integration with other international RD programs from the countries mentioned above, helping to uncover the extent to which non-coding DNA variants play a role in disease.

Right from the start of the project WP7 will pursue, in parallel, a distributed and a federated re-analysis approach. **In Years 1-3**, the Solve-RD based reanalysis pipeline will be upscaled for existing short read exome and genome datasets from ERNs, using reference GRCh38 and relying on WP15 to develop portable virtual research environments and pipelines to facilitate the federated reanalysis approach. This will be used for the design and implementation of a first federated reanalysis network which will be facilitated through meetings with representatives from countries not able to submit data to the ERDERA distributed infrastructure, as well as through participation in 1+MG discussions and leveraging the GDI network. Of note, although the CRN-Diagnostic workstream, and more specifically WP6 and 7 (with support from WP15), is anticipated to leverage GDI developments and GA4GH standards such as Beacon and htsget, as well as MatchMaker Exchange, the CRN focusses on solving the genetic aetiology underlying RD of individual patients, being an ERDERA workstream, not driven by GDI and/or 1+MG. Later, as the project advances, the CRN will move predominantly into federated analysis sharing data-analytical tools and coordinating interpretation with initially EU-partners from Sweden and France, but later also with partners non-EU partners i.e., Canada, United Kingdom, and Australia, while considering ELSI-related aspects, and aligning with WP25 on further internal capacity building. In coordination with WP8, WP7 partners will test and incorporate other innovative types of genomics data (such as long read genomes, LRS), analysis methods and interpretation approaches, such as the integration of other -omics data to enhance diagnostic yield, and with support of WP16 novel avenues of (AI-based) phenotype collection, including antenatal phenotypes, will be explored to optimize diagnostic outcome.

Dissemination of results will be achieved via publications, as well as upload of pathogenic variations to international databases (in collaboration with WP6.3). Moreover, implementation guidelines on the successful reanalysis strategies will be provided to promote integration into local health care services, alongside the illustration of useful knowledge bases and annotations to provide easy and direct information on and access to therapeutic opportunities (linked to WP12). Finally, training and capacity building will be channelled through WP20, mainly T20.3.

Objectives

The main objective of WP7 is to coordinate a diagnostic research pipeline to re-analyse existing genomic data from undiagnosed RD patients to increase diagnostic yield and reduce time to diagnosis.
The specific objectives for Year 1 are:

- Initiate the coordination of a pan-European genomics diagnostic research pipeline beyond the state-of-the-art diagnostic pipeline.
- Start the re-analysis of existing data following a distributed approach while starting preparations for a federated model to discover novel diagnoses.
- Kick-start the organisation of variant interpretation and the development of best practices to improve this activity across disease groups and ERNs.

Description of Programmed Activities

WP7 will achieve its objectives through 4 main tasks (Figure 1) and collaboration with the other CRN Research Diagnostics stream WPs (WP6 and WP8), the Data Services Hub, ERNs and UDPs. For the transition to a federated approach, WP7 will count initially on the expertise provided by partners from Sweden and France, although it will welcome the participation of partners from other countries, including from outside the EU. Figure 1 provides a schematic representation of WP7 and its main interactions.

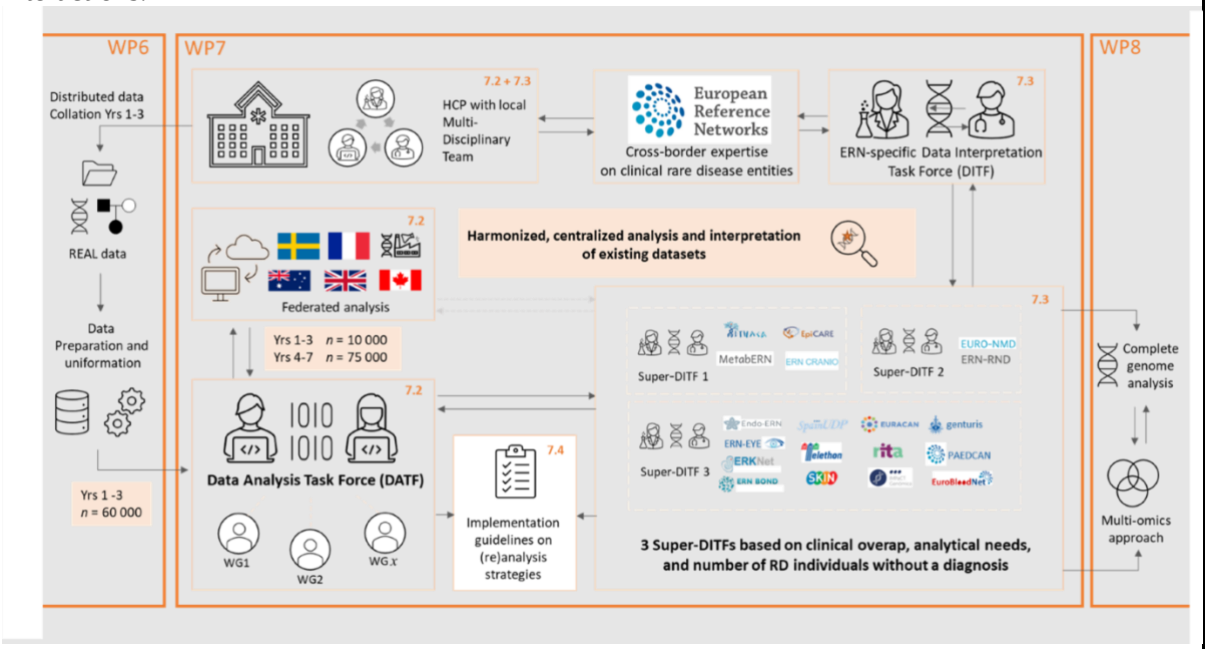
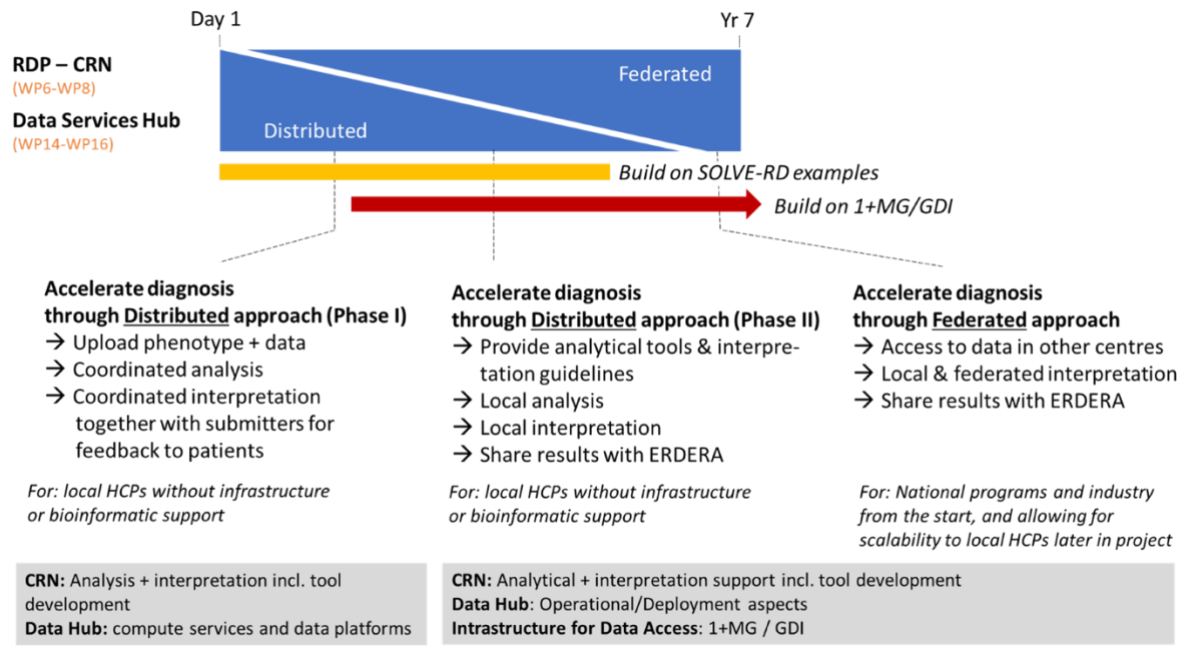


Figure 8. ***Schematic representation of WP7.*** *Work package 7 will consist of 4 tasks together allowing harmonized, distributed + federated analysis and interpretation of existing dataset of individuals with undiagnosed RD, all collected in implementation guidelines on reanalysis strategies in everyday clinical care. Links with WP6, for data collation, and WP8 for innovative genomic applications, are also shown. Black arrows indicate direct interactions/ connections between tasks. Additionally, support is provided by Data Services Hub WP15-16. Light grey dotted arrows indicate indirect interactions for supporting federated interpretation.*

T7.1. Exome and genome re-analysis pipeline coordination and monitoring (M1-M12) *TL: UT, CNAG, SRUMC; Contributors: CHU Dijon, UNEW, UGENT, ISCIII, CAD, UU, CENTOGENE, CHEO-RI*, UMCG, EURORDIS, CIBER.* T7.1. aligns with GO:1; SO:5; OO:2,3,5.
Several task forces, working groups and a committee will be established to coordinate and monitor the activities. One Data Analysis Task Force (DATF) and three super-Data Interpretation Task Forces (DITFs; see T7.3) will bring together the expertise from data analysis and clinical researchers. The DATF will have 3 co-leads, and the super-DITFs will have two co-leads each (see T7.3). They will form the "Pipeline coordination and monitoring committee", which will also include early adopters of

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the federated approach from EU (e.g., Sweden and France) but also from non-EU countries such as Canada, Australia, and UK. The committee will jointly coordinate and monitor the continuously revised CRN standard diagnostic research pipeline for REAL data (e.g. standardized HPO-based phenotypes, pedigree information and genetic data), which should be applicable in both a distributed and federated manner. The starting point will be the Solve-RD re-analysis pipeline using GRCh38 reference genome. The committee will also coordinate and monitor the actual re-analysis strategy (e.g., data freezes, prioritization and monitoring of re-analysis projects, interpretation strategy, participating groups and timelines, summarizing and reporting of results and findings) and engage with other WPs (e.g., WP6, WP8, Data Hub). **In Year 1,** this task will establish the Data Analysis Task Force (DATF), the ERN-specific data interpretation task forces (DITFs) and three super-DITFs and the "Pipeline coordination and monitoring committee" (Figure 1). The leads of these task forces will decide the first



priorities and set up the first working groups, as well as the organisation of the consultation approach to enable participation of relevant stakeholders and a fair decision-making process. The objective is to prioritise the activities, determine analytical pipelines and interpretation strategies. While the focus will be initially the distributed approach, the task will also consider, in collaboration with WP6 and the DSH, the federated approach from the start to ensure that the activities can be transitioned to that model as soon as possible (see Figure 9).

Figure 9. ***Schematic representation of shift from distributed to federated approach.*** *The ultimate goal is a federated approach for reanalysis of existing data to facilitate new diagnosis. At the start of the project, however, a federated approach will not yet be possible requiring a distributed analysis of data. The CRN and Data Services Hub will collaborate on providing operationality and deployment aspects for a federated approach and will also closely align with B1+MG/GDI.*

T7.2. Standardised exome and genome re-analysis beyond state-of-the-art diagnosis (M1-M12) *TL: CNAG, CAD; Contributors: UT, SRUMC, UU, CENTOGENE, CHEO-RI*, UMCG, INSERM_Orphanet, CIBER.* T7.2. aligns with GO:1; SO:1,4,5; OO:1,3.
In Years 1-3, the distributed Solve-RD-based standardized research re-analysis of REAL data from unsolved cases (including relatives, as available) will be upscaled. Facilitated by planning and internal developments and pilots (WP6, WP15) as well as 1+MG/GDI advances in Years 1-3, the federated research re-analysis approach will predominantly be used from Year 4, at the latest. The pipeline used will be coordinated in T7.1 and developed in T15.2 for easy portability, key for both a distributed and a federated approach. The distributed analysis will be done initially in 3 main Solve-RD clusters (CNAG, UT, SRUMC) and the RD-Connect GPAP. Other clusters and platforms will be able to join

for the distributed or federated approach after evaluation and approval by the T7.1 Committee, taking also into consideration T13.1 evaluation on technical requirements and VP specifications compliance. T15.3 will take care of piloting use cases for federated analysis. The first 18M will focus on exome re-analysis, moving to srWGS afterwards and including long read genomes later one (informed by WP8). In line with this, the initial focus will be on coding regions, with an increasing focus on non-coding regions. The analysis will include all types of genetic variants (SNVs/InDels, somatic/mosaics, mtDNA, SVs in general like CNVs, STRs and MEIs).

In Year 1, the aim is to analyse the first 7500 REAL datasets (mostly exomes) in a distributed fashion for all variant types (basically in coding regions), as well as to evaluate federated data strategies for re-analysis operations with partners requiring federated approaches, including industry. The output will be periodic reporting of selected variants to DITFs in T7.3 for interpretation; methods for filtering may include information derived from matched (multi-)omics analyses or (AI-based) phenotypic-similarity, including antenatal phenotypic information (WP16). The workflow will rely on a system developed and served by T15.2 to deliver the variants to the DITFs where they will be able to provide feedback.

T7.3. Innovative exome and genome re-analysis (M7-M12) *TL: SRUMC, ISCIII; Contributors: CHU Dijon, UGENT, UNEW*, CENTOGENE, RS, GMS-RS, IMAGINE, CHEO-RI*.* T7.3. aligns with GO:1; SO:1,4,5; OO:4,5.
In this task, all REAL datasets of individuals with RD of unknown genetic origin will be re-interpreted using the results from T7.2 with the main aim to find new diagnoses to be reported back to the individual RD patients. To allow for efficient interpretation, and uniformity across all disease groups, 3 super data-interpretations task forces (super-DITFs) will be installed. Each super-DITFs is responsible for multiple disease groups/ERNs, which will be combined based on overlap in clinical spectra, such as for instance ERN ITHACA, EpiCARE, ERN CRANIO, and MetabERN, as well as Euro-NMD and ERN-RND, or based on national undiagnosed disease networks/programmes, such as for UDP Spain, CIBER-ER Spain and FTELE and/or requiring similar analysis strategies such as rare cancers. DITF-leads will coordinate with data analytical task forces (DATFs) on processing of REAL data sets and feedback of results. Initially, focus will be on distributed interpretation of known disease genes and existing exome and short read genome datasets, as has also successfully been done in the Solve-RD project. With access to large datasets, novel disease genes will be sought by innovative statistical approaches and paradigms other than classic monogenic disease as well as novel variant prioritization algorithms via federated approaches. When available, analyses and interpretation will also involve other omics datasets such as long-read genomes (contributing partners for existing datasets and WP8 for novel datasets). The main activities for T7.3 are:

- Plan and implement variant interpretation to diagnose RD patients: from a distributed to a federated approach and using (AI-based) prioritization tools on both genotype and (standardized) phenotypes.
- Evaluation of genetic variants (provided by analysis WGs) by DITFs members in the clinical context and providing the new diagnosis to the patients with RD.
- Share expertise between DITFs/ERNs and contributing partners.
- Develop best practices for routine variant interpretation.
- Co-develop and test additional interpretation approaches with the DATF and WGs Joint data re-analyses across ERNs and UDPs (e.g., for novel gene discovery, and alternative inheritance patterns) and other large databases on RD (e.g., Care4Rare, DDD).
- Development and application of novel analyses methods not yet part of the best practices for routine variant interpretation approaches, including non-coding variation.
- Functional validation to prove pathogenicity of variants for known and novel disease-genes.

In Year 1, T7.3. will suggest DITF leads for the individual ERNs and UDPs from all participating centres (overview of centres in WP6), which will be consolidated by T7.1. In addition, leads of 7.3 in coordination with WP6 and ERDERA ethical and legal experts, provide support to local HCPs in ELSI- and IRB challenges related to data sharing, using best practice examples from the solve-RD project.

This is a key activity to ensure that data made available for re-analysis is then also available for distributed or federated interpretation. T7.3. will also initiate the interpretation of the first 7,500 REAL datasets analysed in T7.2. and will determine the best interpretation strategies per variant type. Also, in preparation of the inclusion of antenatal phenotypes, WP7 will link to WP6 and WP16 to determine a proof-of-concept use case on the use of antenatal phenotypes.

T7.4. Propagation of knowledge and best practice guidelines (M1-M12) *TL: KU Leuven, INSERM_U974; Contributors: CAD, IBG, ISCIII, SRUMC, EURORDIS, CNAG.* T7.4. aligns with GO:1; SO:1,2; OO:1.
The CRN-diagnostic workstream requires translation of the most successful approach into clinical service at healthcare institutes. To advertise the work of WP6, WP7 and WP8 and incite people to adapt the re-interpretation tools and novel technologies, guidance is needed. In practice, the outcome of T7.2 and T7.3 must be captured in best practice guidelines, and the instructions must be matched with the needs of the potential users in the clinical diagnostic centres, and with international ISO-norms for medical laboratories, IVD-Regulation, GDPR and regulatory requirements. 'Guidelines for diagnostic next generation sequencing' and 'Recommendations for whole genome sequencing in diagnostics for RDs' have been issued in 2016 and 2022 respectively, under the auspices of the European Society of Human Genetics (ESHG) and EuroGentest. The experience will be used to provide user-oriented implementation guidelines. Stakeholders will be reached out via the National Mirror Groups (WP23), and training to the community will be provided via T20.3.

To shorten the pathway to diagnosis and to treatment, two translation tools will be targeted. First, the identification of molecular diagnoses may provide (in)direct leads for therapeutic strategies in n=1 or n=few trials (WP12). To readily identify genes and variants amenable to such therapeutic strategies, links with other repositories and annotation are required, such as knowledge on the Treatabolome (WP16) and/or other actionable variants. Second, it is important to illustrate the usefulness of knowledge base and ontologies (WP16) by assessing how they perform in clinical context. The goal is to warrant that ORPHAcodes and other tools are used in the clinic, right from the start of the diagnostic process. Finally, there is a need to evaluate the use of the above, and to identify future bottlenecks in the real world. T7.4 will therefore focus on two entities:

1. Provide implementation guidelines to promote implementation in health care services, including:
    - Description of the protocols developed/used in this WP (WP7, T7.1, T7.2 and T7.3), in WP6 (data availability), and with an outlook towards WP8 (genomic innovation to shorten tile to diagnosis) and towards RD maps (T16.4 in WP16: knowledge bases and ontologies).
    - Compilation and integration of (inter)national guidelines on variant interpretation for use in clinical diagnostics (based on approaches and output of T7.2 and T7.3).
    - Evaluation of legal implications of variant interpretation in a clinical setting while defining the legal status of interpreted data in relation to the (electronic) medical record of patients.
    - Evaluation of cost-effectiveness of clinical reanalysis of existing datasets (based on approaches and output of T7.2 and T7.3).
2. Illustrate the usefulness of knowledge bases and ontologies and evaluate how they perform in a clinical context, including:
    - Explanation of (the links to) treatabolome, MAxO ontology, therapeutic trials, etc. (Link to WP16 knowledge bases and ontologies T16.3).
    - Promotion of the use of ORPHACodes and other ontologies directly right from the start in clinical practice and the evaluation of the yield of these tools (link to WP16 T16.5).

In Year 1, TLs of T7.4 (or delegated thereof) will witness the processes starting in T7.2. and T7.3 for informed initiation of the T7.4. specific tasks in Year 2.

Additional deliverables *(additional to those included in part B of the proposal)*

None

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Set of Activities Number	**8**		**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Diagnostic Research Workstream - Genomic innovation to shorten time to diagnosis**						
Short name of participant & (No)	SRUMC (11)	VULSK (27)	TUM (12)	UT (8)	UMCG (6)	CCRI GmbH (42)	MUH (81)
Person Months	33	6	21	4.5	3	6	6
Short name of participants & (No)	UCL* (174)	CUH* (171)	CHEO-RI* (152)				
Person Months							
Start month	M1		**End month**		M12		

**Associated partners providing in-kind contribution*

State of the art behind this WP

This WP will enable the most innovative (gen)omics approaches for RD diagnostics and research. This WP consists of two parts: 1) the envisioned work will lead to a more complete understanding of RD by a truly complete human genome analysis, 2) new innovative transcriptomics and other -omics approaches shall drastically improve the variant interpretation for RD. These innovations will change diagnostics of RD significantly and shall enable a molecular/genetic diagnosis for the very first time for so far 'unsolvable diseases', and shall individually or jointly shorten the time to an RD diagnosis. This WP shall demonstrate how the innovative methods applied shall set new standards, by providing a truly generic approach by long-read genomes to all RD with a significantly reduced turn-around time, compared to currently practiced cascade testing. This shall thus make RD diagnostics more generic, remove redundant workflows, and ultimately result in more economic, rapid, and successful RD diagnostics.

Exome and genome sequencing are being used as the standard of care diagnostic assays for RD. However, recent efforts have shown that even short-read genome sequencing data are incomplete and miss a significant proportion of clinically relevant variation. Here, WP8 aims to utilize (provided/matched as well as newly produced) latest long-read genomics methods, to a) identify so far hidden variants; b) ultimately provide a generic genome test that allows full resolution of all variants to the benefit of all RD patients.

In parallel, WP8 will utilize the latest transcriptome, epigenome and other -omics technologies that are provided by all partners (WP6-8). These shall assist to pinpoint the disease-causing variants from complete genome analyses. This will warrant reducing the VUS (variants of unknown significance)-challenge significantly and set new standards in variant interpretation for RD research and diagnostics.

As for WP6 & WP7, WP8 aims to bring expertise and data together, but also to produce new data with latest technologies, especially enabling clinics and laboratories in underrepresented countries to have access and knowledge faster in turn achieving faster RD diagnoses. WP8 will have very close interaction with many ERDERA partners, with strong emphasis and interaction WP6&7; e.g. any innovation that benefits the move from distributed to federated analyses shall benefit WP6-8. The return of results to referring clinicians and thus patients in WP8 will benefit from methods deployed in WP6 (T6.3).

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Methodology

Here, WP8 aims to use the consortium's expertise as pioneers in genomics, in particular in long-read genomics and multi-omics data integration technologies. The first part entails both leading long-read sequencing (LRS) platforms nanopore sequencing (ONT, Oxford Nanopore Technologies, UK) and HiFi sequencing (PacBio, USA) as well as optical genome mapping (OGM, Bionano, USA); each enabling to detect missed or hidden variants, in particular structural variants, that escape short-read methods.

LRS furthermore enable a complete human genome analysis as recently demonstrated by the T2T consortium (Nurk et al. Science 376,44-53(2022)), including highest sensitivity to all variant types (SNV, InDel, SV, STRs, etc.), with demonstrated utility to detect de novo mutations of all kinds (Kucuk et al. Genome Med. 8;15(1):34 (2023)). This also allows access to “dark regions” of the human genome that were largely inaccessible, including highly homologous sequences and genes with pseudogenes. LRS also allows for phasing and assembly - ultimately allowing the near-perfect genome analysis, which shall speed up diagnostics for many RD in the future. One additional feature of LRS is that DNA-modifications can be detected, DNA-methylation which shall be utilised in this WP (epigenome analysis). The goal is to provide a fully complete and generic workflow for all RD patients, resulting in significantly accelerated RD diagnoses and the most impactful diagnostic innovation for RD ever.

WP8 will optimise and apply tools that go beyond the DNA level, and connect leaders in genomics and multi-omics analyses with RD experts to improve RD diagnoses and deliver tools and expertise to our partners. Strong focus will be on transcriptome (short and long-read RNA-seq datasets) and epigenome data (existing and produced here as part of the long-read genomes). This data will reveal gene regulatory aberrations helping the functional interpretation of genetic variants. Here too, efforts will be made in monitoring and continuously improving time spent at every step of the diagnostic chain. All pipelines, software developed and tested here shall be released (see milestones and deliverables), and releases shall be coordinated in collaboration with the Data Service Hub (DSH), furthermore WP6-8 shall interact closely with DSH for any innovations to integrate patient data (phenotype HPO, EHR, etc) that can be integrated with genomic and other data from WP6-8 (RD-REAL).

Objectives

The main objective of this WP is to establish the most innovative diagnostic approaches for RDs to enable a significantly shorter diagnosis time. The innovations provided here shall provide truly generic genomic analyses by full genome analysis and interpretation, accelerating RD diagnostics throughout Europe. The significantly improved diagnostic yield of RDs, will be crucial to make more RD families amenable to actionability, therapy and improved care.

In Year 1, our objectives will cover initial steps:

- Enabling Access Of Complete Genome Sequencing For RDs. In Underrepresented Countries
- Enabling Complete Genome Sequencing And Analysis For RDs. To Shorten Time To Diagnosis
- Enabling Complete Genome Mapping Data
- Establishing New Genomics (Transcriptomics) Analysis Capabilities
- Establishing New Multi-Omics Data Integration Approaches To Shorten Time To Diagnosis.

Description of Programmed Activities

T8.1. Enable inclusion of underrepresented countries into innovative RD diagnostic research (M1-M12) *TL: MUH, VULSK, Contributors: SRUMC, TUM, CNAG, UT*. T8.1. aligns with GO:1; SO:1,2,4; OO:1-4.
This task aims to connect European and global RD clinicians even more, by fostering the reach of scientists and patients from underrepresented countries. This task will actively collaborate with WP23

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and WP24, and RD diagnostic centres shall be identified via National Mirror Groups. WP8 contributors will specifically aim to educate a network of RD-experts in selection of RD patients and families to demonstrate the revolutionary impact of long-read genomic technologies. This task will coordinate the case and sample selections for the use cases in T8.2. and T8.3. All sample selections will benefit from ethics and regulatory advice and support in respective ERDERA dedicated WPs/tasks. This capacity building connects all European RD experts, leads to the best RD case selection and a strong demonstration of new diagnoses in so far undiagnosed RD, and significantly faster diagnoses in general. This task will coordinate the case and

The RD network across Europe will be initiated with emphasis to involve clinicians, scientists and patients from underrepresented countries in Year 1: with jamborees/meetings to explain use cases for long-read sequencing (LRS) and optical genome mapping (OGM), develop case selection instructions, and arrange biomaterial shipment for first long-read technologies batches form underrepresented countries. Moreover, the first training and education actions in selection of RD patients and families will be performed, but also educate on the use and outcome of long-read technologies for the use cases in the T8.2 and T8.3. Notably, MUH will organize one RD jamboree in person (F2F), additional efforts will utilize online platforms in collaboration with VUHSK.

T8.2. Enable complete long-read genome sequencing and analysis for RD to shorten time to diagnosis (M1-M12) *TL: SRUMC, UT; Contributors: UMCG, CHEO-RI*, TUM, CNAG.* T8.2. aligns with GO:1; SO:1,2,4; OO:1-4.

This task aims to provide RD-optimized long-read sequencing (LRS) pipelines to the RD community. These shall be tested on selected use cases (close interaction with T8.1), and guarantee respective bio-sample readiness, to provide evidence that LRS will diagnose a significant proportion of undiagnosed RDs, and significantly reduce time to diagnoses. The use cases data shall be analysed by our LRS experts (DATF) and shared in manageable forms with the respective disease experts (DITF/ERN). Ultimately the tests, and analysis pipelines developed here provide a truly generic germline genetic test for all RDs that can innovate diagnostics across Europe (and associated countries).

In Year 1, the long-read sequencing readiness for RDs will be established. This will mean that strategic partners within CRN network will be explored to provide (cost-)effective and timely long-read sequencing (based on the two dominant technologies: PacBio and ONT). Also, T8.2. will test and optimize long-read sequencing analysis pipelines for comprehensive RD research (on already available and newly produced data). Moreover, T8.2. will work towards the inclusion of first use-cases. Notably, the first new data production for RD cases selected from underrepresented countries will be generated. The partner SRUMC will organize and hold a face-to-face DATF meeting for long-read sequencing. Under best circumstances LRS will already contribute to solving undiagnosed RD cases – showcasing the more effective diagnostic potential for the next years.

T8.3. Enable complete genome mapping for RD to shorten time to diagnosis (starts M13) *TL: SRUMC, UCL; Contributors: TUM, CNAG, UT.* T8.3. aligns with GO:1; SO:1,2,4; OO:1-4.

This task aims to provide RD-optimized ultra-long-read optical genome mapping (OGM) pipelines to the RD community. These shall be tested on selected use cases (close interaction with T8.1) and guarantee respective bio-sample readiness (T8.2), to provide evidence that OGM will diagnose a significant proportion of undiagnosed RDs, and significantly reduce time to diagnoses. The use cases data shall be analysed by our OGM experts (DATF) and shared in manageable forms with the respective disease experts (DITF/ERN). The long-read tests, analysis pipelines, and tests developed here, shall demonstrate the added value of long-read technologies aiming towards a holistic genome analysis that can innovate diagnostics across Europe (and associated countries). This task is complementary to T8.2, and in part can de-risk aims of T8.2. In case some European countries cannot follow a generic LRS test for RD, the combined effort of standard exome/genome analysis with OGM may also provide a ‘near perfect RD genome analyses. Hence, this task also adds to the democratisation of RD diagnostics.

In Year 1, the WP leaders will make the first step into optical genome mapping readiness for RD, e.g. T8.3. will explore strategic partners within CRN network to provide (cost-)effective and timely OGM data production. Specifically, the WP8 contributors will comparatively assess and identify potential

partner(s) to generate the optical genome mapping data within the CRN network and prepare pipelines for comprehensive data analysis of structural variants (SVs) based on already available data within CRN. WP 8 contributors shall provide instructions/SOPs for biomaterial shipment based on use cases defined in T8.1.

T8.4. New genomics (transcriptomics) analysis capabilities to understand genetic variation in RD (M1-M12) *TL: TUM, CCRI GmbH; Contributors: CUH, IBG, CNAG, SRUMC, UT*. T8.4. aligns with GO:1; SO:1,2,4; OO:1-4.
While, in principle, the information about the genetic disease causes lies in the DNA, the functional interpretation of all genomic variants of an individual remains difficult, notably for non-coding variants. By probing directly regulatory impact regarding the expression levels and the integrity of mRNA sequences (e.g. altered through aberrant splicing), bulk RNA-seq analysis has emerged as a powerful complementary approach to genome analysis for pinpointing genetic causes of RDs. In addition, the recent advent of single-cell RNA-seq (scRNA-seq) approaches in RD provides another layer identifying cellular heterogeneity and gene expression dynamics, enabling the identification of key, cell type-specific molecular players and aberrant developmental trajectories in RD, as recently demonstrated for inborn disorders of haematopoiesis or immune system development. T8.4 have established RNA-seq analysis pipelines for RD diagnostics and successfully used it in the project Solve-RD, that can be a solid foundation for further development. However, more work is needed to truly integrate DNA analysis with both bulk- and scRNA-seq, monitor and improve the time to diagnosis, and increase the robustness and the between-lab comparability of results. So far, aberrant expression and splicing are called from the RNA-seq samples, and the genetic variants are reinvestigated a posteriori. Here, T8.4. will develop integrative methods that jointly process DNA variants and RNA-seq data to increase analysis speed and reliability. Additional integrations of scRNA-seq data will directly provide insight into the disease biology and further improve the identification of disease-causing variants by identifying specific cell types and cellular and developmental processes affected by genetic lesions, with relevance to unsolved RD patients. Tools predicting variants affecting splicing (e.g., SpliceAI, AbSplice) will be integrated along with aberrant splicing callers. The same will be considered for aberrant expression (e.g. using Enformer). Moreover, T8.4. will develop methods leveraging variant phasing obtained from long-read sequencing and mono-allelic expression (of rare and common variants) to establish cis-regulatory impacts or rare variants. Also, coherent interpretation guidelines will be developed and regularly revised in coordination with data interpreters. Interfaces will be developed to improve the speed, quality, and consistency of the decisions according to these guidelines (e.g., via structured web reports, controlled vocabulary, decision tracing). As successfully implemented in Solve-RD, T8.4. will offer expert call-in hour as well as regular jamboree events (so-called “Solvathon”) in which training and actual data analysis are done in groups. T8.4. will record diagnostic rate statistics by aberrant transcriptome event types (splicing, mono-allelic expression, expression levels) as well as the dates of i) sample collection, ii) sequencing, iii) bioinformatics pipeline completion, iv) bulk-/scRNA-seq results interpretation, and v) diagnostics to identify bottlenecks and prioritize process improvements for shortening time to diagnosis. All code, training material, and guidelines will be made publicly available.

In Year 1, WP8 contributors will deploy state-of-the-art RNA-seq pipeline in pilot compute-centres (e.g., DROP, Yepez et al, Nature protocol, 2021). This will allow (re-)analysis of available matched DNA-RNA datasets of RD cases, via WP6&7. Also, the format for sharing the necessary sample metadata (sample annotations) will be agreed and designed.

T8.5. Multi-omics data integration to shorten time to diagnosis in RD (starts M13) *TL: TUM, AMU; Contributors: CCRI GmbH, OPBG, REGIONH, SRUMC, CNAG, UT*. T8.5. aligns with GO:1; SO:1,2,4; OO:1-4.
RNA-seq based diagnosis as in T8.4 focuses on pinpointing so-called cis-effects, i.e., the effects of the genetic variants on transcription, splicing, or degradation of the very gene the variants are located in. However, the functional impacts of variants with strong phenotypic consequences do not stop at the immediate gene it belongs to. The development of a disease impacts many omics scales, from the

expression levels of further genes to epigenetic modifications, protein, and metabolite abundance, among other. Partners of this project collect such omics data on patient samples alongside patient phenotypes using controlled vocabularies (HPO). Moreover, complementary to patient-specific data, two decades of functional genomics research have produced a wealth of knowledge and experimental data in model systems about gene function and interactions that can and shall be integrated to accelerate time-to-diagnosis. The goal of this task is to develop, assess, and apply new modelling techniques integrating multiscale omics data layers and patient-related information to better pinpoint genetic causes of RD phenotypes. To this end, AI techniques specifically dedicated to heterogeneous data integration, such as joint dimensionality reduction and graph embedding techniques (e.g., MultiVERSE, momix), which offer the needed scalability and mathematical expressivity will be employed. A strong focus will be set on exploiting epigenomics data whereby so-called epi-signatures from existing epi-array data will be first investigated transitioning toward using long-read genomic data that will be produced over the course of the project and which also reveal DNA methylation (T8.2). **In Year 1**, the WP leaders will perform the first investigation of multi-omics application of RNA-seq and phenotype of existing samples. This will include developing the first version of an algorithm integrating epigenomics signatures with phenotype.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**9**		**Start Date or Starting Event**		**M1: September 2024**	
Set of Activities Title	**Outcome Research Workstream - Real World Data**					
Short name of participant & (No)	UKHD (13)	SRUMC (11)	VHIR (15)	APHP (24)	Erasmus MC (53)	UPM (18)	KUM (136.1)
Person Months	50	12	9	18	5	4	5
Short name of participant & (No)	UT (8)	LUMC (16)	Sciensano (97)	INSERM _U1112 (UNISTRA) (1)	C-Path (14)	UKLFR (115)	DDF (51)
Person Months	9	9	10	2	24	8	8
Start month	M1		**End month**		M12	

State of the art behind this WP

In RD research, data collected under real-world conditions are critically important to inform disease demographics, identify the disease-specific needs for innovative therapies, explore the patterns and determinants of disease evolution under the current standard of care, model the effects of interventions on outcomes, provide reference data for clinical trial programmes, and identify patients for clinical trials. EMA recently acknowledged the need to complement clinical trial information with RWD, provided a guideline for regulatory-quality data collection and set up the Data Analysis and Real-World Interrogation Network (Darwin EU). The advent of the European Reference Networks (ERN) and the formation of ERN-wide registries, accompanied by the emergence of national and patient-driven RD registries, have created unprecedented potential to facilitate therapeutic innovation at multiple levels. However, the collection and research utilization of RWD still faces significant obstacles all along the value chain, from primary data capture to cohort integration, efficient data analysis and clinical trial-ready data provision. Numerous technical, legal-regulatory, and methodological issues need to be solved to overcome these challenges. WP9 will utilize the unique

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facilities and support expertise available within ERDERA to create, integrate and process real-world RD cohort data towards clinical trial readiness.

Methodology

This WP will utilize the unique facilities and support expertise available in the ERDERA to create and process real-world RD cohort data towards clinical trial readiness. Several case / proof-of-concept studies, selected according to thematic complementarity and feasibility, including the involved partners' expertise, data readiness and relevance for therapeutics development, will be performed. They will paradigmatically highlight the challenges of RDs outcome research and develop generalizable solutions with methodological support from the service infrastructures provided to the CRN. Each case study will cover one or several tasks along the research and innovation value chain.

Both structured and unstructured Electronic Health Records (EHR) data captured across different IT systems and European languages will be processed with the help of Natural Language Processing experts for incorporation into registries and other outcome research project databases. In coordination with Data Services Hub specialists, innovative strategies will be formulated for population-based outcome research. These strategies will harness secondary health care and social security data integrated with registries, with an emphasis on crafting guidelines to produce FAIR-compliant population datasets. The focus is on creating a universally applicable, interoperable dataset anchored on linked European Reference Network (ERN) registry and social security data. By liaising with regulatory institutions, it is anticipated that this dataset will gain wider acceptance.

The advantages of merging existing RD patient cohort data will be highlighted in several case studies, leveraging also on the Data Services Hub expertise, with the objective to craft robust reference groups, poised to serve as benchmarks for upcoming clinical trials.

Procedures for academia-driven patient registries and natural history studies will be established during the sequential stages of engagement with regulatory authorities. The aim is to secure EMA qualification for regulatory-grade natural history registry data for potential utilization as external comparator arms in non-randomized clinical trials in RDs. Additionally, these procedures are designed to assist in post-authorisation safety surveillance (PASS) and efficacy (PAES) studies.

Lastly, existing model-building technology will be utilized, and new methodology will be developed to demonstrate the creation of Drug Development Tools (DDTs). These tools aim to enhance the comprehension of RD progression patterns and facilitate quicker, more certain, and cost-effective predictions regarding the effectiveness and safety of new products. The C-Path Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP®) will be leveraged as a central, standardized infrastructure to support and accelerate RD characterization. This will be aligned with DDT development projects scheduled in parallel for future IHI project calls, ensuring thematic coherence. Expertise in operational and regulatory aspects will be sourced from WP14 & WP18.

Objectives

The main objective of the WP is to augment the trial readiness of RWD available to the CRN partners.
The WP will serve the following specific objectives:

- To lead the way to efficient retrieval of primary healthcare data for RD outcome research;
- To demonstrate successful utilization of population-based data for RD outcome research;
- To generate powerful reference patient cohorts by integration of data sources;
- To collect and make available regulatory-grade natural history reference data;
- To demonstrate how to model and explore predictors and effectors of disease progression in RD patients;
- To develop a platform for clinical trial simulation of RDs.

The objectives of the WP 9 for the Year 1 are:

- To make multiple RWD data sets available for data integration;
- To optimise the data quality of available data sets;
- To establish the legal and formal prerequisites for extraction of primary healthcare data.

Description of Programmed Activities

T9.1. Use of primary healthcare data for RD outcome research (M1-M12) *TL: SRUMC; Contributors: VHIR, APHP, Erasmus MC, UPM, LMU, KUM.* T9.1. aligns with GO:2,3; SO:2,5; OO:1,2.
In this task, structured and unstructured EHR data will be extracted and prepared for re-use in registries or other databases in outcome research projects. In close collaboration with T14.2 partners, Natural Language Processing (NLP) will be applied to unstructured data. This task will benefit from ongoing activities of the beneficiaries, and existing coordination activities by the ERNs. The following disease groups will be studied: urogenital anomalies, neuromuscular disorders, craniofacial anomalies, developmental and epileptic encephalopathies, rare anaemia disorders, and mitochondrial disorders.

In Year 1, T9.1. will create an inventory of the current routines (automated or manual) for data extraction from EHRs with the participating beneficiaries, the data use conditions given the consent of the patients, GDPR and the applicable national laws, the available tooling (including NLP and pseudonymization tools), and an assessment of the FAIRness of the available software tools. If required, T9.1. will start the procedures to obtain ethical approval from the institutional review boards and perform a data protection impact assessment.

T9.2. Use of population-based data for RD outcome research (M1-12) *TL: APHP; Contributor: Sciensano, UKHD.* T9.2. aligns with GO:3; SO:2; OO:2.
In this task innovative approaches to empower population-based outcome research, based on secondary use of health care or social security data linked to registries, will be developed in three case studies in collaboration with data service hub experts to derive generic guidelines to build FAIR population-based data.

In **ST19.2.1.**, a use case addressing the neurodevelopmental disorder Dravet syndrome, the French National Rare Disease Registry (BNDMR) and French social security data and the National System of Health Data (SNDS), as well as a disease specific national registry in Italy (RESIDRAS) will be accessed to study in two countrywide samples the impact of available drug therapies on life expectancy and healthcare costs. Both cohorts will be shared with the emerging European registry of ERN EpiCARE. **In Year 1,** ST19.2.1. will select relevant variables from RESIDRAS registry to assess the impact of drugs on life expectancy and healthcare costs. ST19.2.1. will then request access for equivalent variables to regulatory bodies for data on patients having Dravet syndrome in the National Health Data System linked with data from the French National Rare Diseases Registry.

In **ST9.2.2.**, national health insurance data of patients with Hirschsprung disease will be linked with outcome data (inc. PROMs) collected nationwide in Belgium and combined with equivalent national healthcare data collected by BNDMR and SNDS in France for a comprehensive analysis of the impact of disease phenotype and care pathways on health outcomes. The data collected in both countries will be shared with the European registry of ERN ERNICA. The experience generated in both STs will be summarized and made available to the ERNs and the RD community at large. **In Year 1,** ST9.2.2. will build the registry for Hirschsprung disease and decide on the variables to collect considering the ERN ERNICA registry. In addition, a collaboration with IMA/AIM (assembly of BE mutual insurance companies) will be set up to investigate which data could be obtained from this organization. Finally, ST9.2.2. will draft a questionnaire for outcome measures and PROM/PREMs in collaboration with different stakeholders such as patient organizations, HCPs, and other relevant stakeholders. Legal documents for the set-up of the registry, for receiving data from IMA/AIM and for the collection of outcome data/PROM/PREM directly from patients will be prepared and submitted for approval. We will also request access for equivalent variables to regulatory bodies for data on patients with

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Hirschsprung disease in the National Health Data System linked with data from the French National Rare Diseases Registry. In conclusion, **in Year 1,** the focus will be on investigating how we can collect data (software, data storage, FAIR characteristics, etc.) and how this data can be linked in one common database (harmonization of pseudonymization, storage of data from different sources, etc.).

ST9.2.3. will combine ERDERA expertise and ERN registry data to develop a pathway for evaluation of the long-term benefits and harms of population-based newborn screening (NBS). A generic NBS module with controlled vocabularies and ontologies will be developed in collaboration with data modelling experts in WP13 and 14, enabling AI/ML data readiness. The module will be adapted for inherited metabolic diseases and implemented in MetabERN's U-IMD registry, which contains longitudinal RWD from patients diagnosed either pre-symptomatically by NBS or after manifestation of symptoms. This will enable the evaluation of NBS programmes across various screened diseases and EU countries, which will be demonstrated for three paradigmatic disorders. **In Year 1,** based on our previous experience on longitudinal observational studies on NBS cohorts in Germany and in interaction with the Screen4Rare/ERN multistakeholder NBS Platform, MetabERN and other stakeholders, we will develop a generic NBS module with controlled vocabularies, ontologies (e.g. EU CDE with ORPHACodes, OMIM codes, HGVS and HPO, as well as WHO ATC, HMDB, and LOINC) and PROMs for diseases that can be screened. In addition, the module will also include specific NBS-related parameters that are not commonly found in RD registries. This includes information about diagnostic quality, diagnostic process quality, analytical quality, and confirmatory diagnostics. To avoid data fragmentation and duplication, it is our strategy to build the new NBS model in a way that enables integration into existing ERN (and other interoperable RD) registries. To test this procedure, we will specifically adapt the new NBS module for inherited metabolic diseases and will include it in MetabERN's web-based U-IMD registry. Ethics and data sharing approvals will be put in place.

T9.3. Integration of patient cohorts for natural history/standard-of-care reference studies (M1-M12) *TL: UKHD; Contributors: APHP, UT, LUMC, SRUMC.* T9.3. aligns with GO:1,3; SO:2; OO:2,3.
This task will demonstrate the added value of integrating existing RD patient cohorts using the services of the ERDERA data hub to create powerful, high-quality reference cohorts for future clinical trials. Four case studies will be performed in important disease areas where clinical trials may be initiated in the lifetime of the ERDERA:

- Three existing regional registries from Italy, Germany and France will be joined with the ILIAD registry of ERN ITHACA and a national French cohort to create a single large natural-history cohort of "RASopathies". The ILIAD registry, built within the ITHACA network by the bioinformatic department of partner MCUG, has been elaborated on a mixed federated model and its beta version is technically finalized with the core EU dataset and genetic/genomic dataset. The final structure of its extension to the constitutional RASopathies sub-registry will be frozen in fall 2023. It includes longitudinal data and treatment information. Legal issues that currently delay access to the core registry are being worked out to meet all GDRP requirements. **In Year 1,** the main objective will be to open access of ILIAD to the ITHACA network and to initiate the transfer of the content of the existing national registries to the ILIAD registry, which will require data dictionaries mapping and transposition, data mining and data curation. In parallel, existing informed consent information will be reviewed, and when necessary, consent for pseudonymized data integration in the EU database will be sought by contacting the families. Strategies to update individual datasets with information not mapped in the earlier national databases will be elaborated.
- The international PodoNet Registry for congenital and steroid resistant nephrotic syndrome will be integrated with the CNS/SRNS cohort enrolled in the ERKReg Registry of ERN ERKNet and additional local registries. Extracts of the merged dataset, which will comprise sizeable cohorts of all hereditary glomerular disorders, will be made available to form reference populations for first-in-human gene therapy studies in monogenic podocytopathies. **In Year 1,** existing informed consent information will be reviewed, and data dictionaries will be mapped for all registries. Data sharing agreements will be arranged as required. To optimize

data quality, data capture will be extended for missing variables relevant to the merged natural history dataset and outdated datasets will be updated.

- Rare endocrine and bone disease cohorts followed in the EuRRECa/EuRR-Bone registries of ERNs ENDO and BOND will be pooled with several ongoing institutional/national data collections to generate reference outcome data for surgical interventions, e.g., in pituitary adenoma or osteogenesis imperfecta. These reference outcome data can serve as benchmarks for future clinical guidelines as well as intervention studies. **In Year 1,** the individual cohorts will be identified, and ethics and data sharing approvals will be set up. Technical requirements to harmonize and facilitate the different data collections will be put in place and first benchmark analyses can be performed.
- The international TreatHSP Registry for Hereditary Spastic Paraplegias will be integrated with the PROSPAX Registry for spastic ataxias and the ARCA Registry for autosomal recessive cerebellar ataxia, thus allowing to establish a novel unique source of cross-aetiology spastic ataxia (SPAX) diseases now genuinely combining three large international longitudinal registries. In addition, several other data types (imaging parameters, digital mobility measures and molecular biomarkers, genetic markers) will be integrated. This will facilitate innovative progression modelling (T9.5.) and targeted molecular n-of-1 and N-of-few trials (WP12) in these diseases. **In Year 1,** we will establish a mapping table based on the data dictionaries of each of the registries. Available research datasets containing additional outcomes (e.g., imaging parameters, digital mobility measures etc.) will be identified and participant identifiers will be mapped across datasets to allow merging of datasets at patient-level. The registries will be expanded to capture information on treatment conditions to allow inclusion of trial dataset into the existing natural history datasets.

T9.4. Development of a blueprint and inventory of regulatory-grade natural history cohort data (M1-M12) *TL: LMU, KUM; Contributors: UKHD, INSERM_U1112, C-PATH.* T9.4. aligns with GO:2; SO:2; OO:2.
This task will establish the procedures for academic-driven patient registries and natural history studies in the early stages of engaging with regulatory authorities to achieve EMA qualification for regulatory-grade natural history that may serve as an external comparator arm in non-randomized clinical trials as well as for post-authorisation safety surveillance (PASS) and efficacy (PAES) studies. For such EMA qualification procedures and key milestones, academic-driven patient registries and natural history studies must fulfil numerous requirements (regarding coverage, core dataset, governance, quality assurance approaches, completeness of core variables, and others) and must undergo extensive and iterative discussions with EMA`s Committee for Medicinal Products for Human Use (CHMP) and its Scientific Advice Working Party (SAWP). In T9.4 we plan to develop the international mitochondrial registry and cohort study, the international hereditary spastic paraparesis registry and cohort study, the CompCure C3 glomerulopathy registry and cohort study, and the inherited retinal dystrophies registry and cohort study (www.REDgistry.eu) as blueprints.

In Year 1, we will set up an inventory of academic-driven patient registries and natural history studies which have already achieved or are currently applying for EMA regulatory-grade qualification. The respective (external) project leaders will be approached to collect information on their hitherto existing experiences. In parallel, we will map for the four blueprint projects to what extent they already fulfil the EMA requirements (regarding coverage, core dataset, governance, quality assurance approaches, completeness of core variables, and others), and – employing discussions with EMA`s CHMP and SAWP - where amendments and rectifications are necessary.

T9.5. Disease progression modelling and prognostic biomarker research (M13-M60) *TL: UT; Contributors: VHIR, UPM, UKLFR, UKHD.* T9.5. aligns with GO:2,3; SO:1,2; OO:1.
This task will develop and apply innovative RD progression methodology that will permit to predict individual disease trajectories. Paradigmatic disease groups will be studied with partially complementary approaches in three sub-tasks.

ST9.5.1. is a cross-aetiology use case focusing on spastic ataxia diseases (SPAX), a genotypically and molecularly heterogeneous group of >300 ultrarare diseases, which share as a common denominator progressive damage of the spinocerebellar and pyramidal tracts, as comprehensively aggregated in T9.3. This ST aims to develop and validate an innovative statistical toolbox for robust individual and n-of-few disease course prediction in this disease group - including quantification of uncertainty and simulation of treatment-induced deviations - based on clinical and prognostic biomarker profiles (molecular biomarkers, digital-motor datasets, imaging biomarkers, genetic stratifiers), thus allowing multimodal outcome progression modelling and use for trial-readiness in ultra-rare/N-of-few diseases. The results will thus also directly inform n-of-few trials (WP12). **In Year 1,** we will first set up a comprehensive development plan for pertinent statistical models specifically apt to ultrarare diseases and the multisystemic nature of SPAX diseases. This development plan will be designed upfront in close collaboration and iterative meetings with the progression modelling methods experts of WP19. First methods for n-of-1/n-of-few progressions modelling will be started to be developed, and then piloted and optimized for two exemplary SPAX diseases.

ST9.5.2. will address sickle cell disease (SCD), aiming to develop individual risk models to improve disease characterization and health status monitoring, personalize therapeutic approaches and ultimately optimize health outcomes. **In Year 1,** we will develop the study protocol including the collection of end-users (i.e. clinicians and researchers) clinical and technical requirements. This will be done in collaboration with T10.2 to integrate clinical and research data with other type of data collected in WP10 such as PROMs and socio-economic data. Technical requirements will be discussed with WP13 for alignment with the Data Service Hub under T13.1. We will also identify data sets available from ERN-EuroBloodNet members based on previous research projects. In addition to the longitudinal dataset of the rare anaemia ERN registry (RADeep) with more than 600 variables covering clinical manifestations, organ damage, treatments, and laboratory data mapped in OMOP, multimodal information including metabolomic (>1900 metabolites), genomic (SNP microarrays) and radiomic data (>500 cerebral MRIs) is available for analysis.

ST9.5.3 will explore spinal muscular atrophy, using the SMArtCARE registry with longitudinal data from >2000 patients treated with one of the three drugs approved for this disorder. This high-quality longitudinal dataset, which is part of the EURO-NMD registry hub and currently used for regulatory and HTA purposes, will be used to model SMA disease trajectories and to test the reproducibility of clinical trial results in a real-world setting. **In Year 1,** we will identify relevant data elements including genetic data and modifiers, medical history and assessments, and physiotherapeutic tests that will be used to model disease trajectories. Identification of appropriate data elements will be performed in cooperation with experts for advanced statistical modelling (WP19). These data sets will be standardized with reference to international clinical coding systems (e.g. ICD10, ATC). In addition, we will explore the availability of clinical trial data from scientific publications and through direct contact with trial sponsors and align the data with our data elements.

T9.6. Development of a model-based clinical trial simulation platform for RDs (M7-M12) *TL: C-PATH; Contributors: DDF, UKHD.* T9.6. aligns with GO:2; SO:2; OO:1,2.
In this task we will use existing and create new model-building technology to demonstrate the creation of Drug Development Tools (DDTs) that will improve the understanding of RD progression patterns and help predicting the effectiveness and safety of new products faster, with more certainty, and at lower costs. Data from natural history / standard-of-care studies as well as previous clinical trials will be used to develop further prediction models that allow to simulate the effect of therapeutic interventions on clinical endpoints and trial sample size requirements using both conventional and small-population trial designs. Data modelling will be performed with the help of the Data Services Hub (T14.3), utilizing the C-Path Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP®). Two therapeutic areas have been selected for the development of DDTs based on their advanced stage of regulatory milestone achievement and initial modelling experience on the RDCA-DAP platform: Autosomal Dominant Polycystic Kidney Disease (ADPKD) and Duchenne Muscular Dystrophy (DMD).

In Year 1, the legal framework for data sharing with the RDCA-DAP platform will be established. The data re-use conditions defined in the Informed Consents will be reviewed and DCA agreements will be negotiated with the cohort holders. Next, European ADPKD cohorts (including an industry-led RCT dataset of 433 patients, placebo and Everolimus interventional arm) will be ingested, mapped, and curated into the RDCA-DAP platform, and the development of a disease model looking at the relationship between total kidney volume growth and eGFR decline will be initiated. The ERKNet registry (ERKReg) will be leveraged, with regards to the cohort of >3,000 ADPKD patients. Additional information regarding received medications, trial participations, kidney volume measurements and retrospective eGFR information from up to 5 years prior to registry enrolment will be obtained from the investigators to enhance the utility of the cohort for the modelling project. In addition, other candidate rare kidney disease datasets for potential disease progression modelling available in ERKReg will be examined.

In the Duchenne subproject, C-Path and DDF will work on improving the semantic interoperability and expanding downstream analytic power of DMD data through curation and utilization of a common data model and ontologies. DDF will be involved in the requirement specifications for data pre-processing and ML models. Data variables from the DMD database will be mapped from highest priority domains including demographics and functional tests. Requests for new ontology terms will be applied where needed. Next, the remaining variables will be mapped, and ontology terms requested. These steps will be preparatory and necessary to ingest DMD data into the C-Path knowledge graph.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**10**		**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Outcome Research Workstream - Clinical Outcome Assessment**						
Short name of participant & (No)	VHIR (15)	UKHD (13)	APHP (24)	Erasmus MC (53)	UT ((8)	UPM (18)	KUM (136.1)
Person Months	21	21	9	2	8	9	2
Start month	M1		**End month**		M12		

State of the art behind this WP

A clinical outcome assessment (COA) measures how patients feel, function or survive. COA can be used to assess disease progression, severity and determine whether a drug has been proven to provide a treatment benefit. According to the IRDiRC, Report on Patient-Centred Outcome Measures in the Field of Rare Diseases on February 2016, there are five types of COAs: Patient Reported Outcome (PRO), Observer Reported Outcomes (ObsRO), Clinician-reported outcomes (ClinRO), Performance Outcomes (PerfO), and Biomarkers. However, clinical studies both interventional and non-interventional, involving several audiences, do not always and systematically measure COAs self-reported by patients and relatives or COAs that patients consider important or relevant. Patient-centred Outcome Measures (PCOMs) aim to place patients, their families, and carers at the heart of decisions concerning the most valuable criteria in health assessment, rather than leaving assessments solely to clinicians. The incorporation of PCOMs, together with Patient Reported Experience Measures (PREMs) and other types of patient self-reported data as socioeconomic data can have a profound impact on individual risk scores for disease severity and on the relevance, effectiveness,

and safety of drug development. This widely acknowledged concept is supported by various stakeholders, including regulators, industry professionals, HTA bodies, patient organizations, and academia. However, there is an urgent need for a unified approach to gather and incorporate PCOMs, specifically tailored to address the unique challenges prevalent in the field of RDs. Several critical issues require immediate attention: (i) The absence of trial endpoints and designs that are acceptable to regulatory authorities and are grounded in concepts and health impacts relevant to patients. (ii) The development of methodologies that are robust, efficient, and compliant with legal, technological, and regulatory requirements, while capitalizing on the latest advancements in health technologies, to collect patient input effectively. (iii) The creation of a comprehensive quantitative assessment of the socio- economic impact of RDs, which would provide policy makers with vital insights to make well-informed decisions and allocate resources appropriately.

Substantial advancements have been achieved by numerous academic consortia and public-private partnerships in various critical areas of patient-centric approaches. These notable milestones include the establishment of frameworks for engaging patients, guidelines for systematically incorporating structured patient input into decision-making processes, and the creation of a repository of PCOMs/ PROMS in RDs. Now, a collaborative effort among all relevant stakeholders aims to propel these achievements further and adapt them specifically for RDs.

Methodology

In this WP we will address key challenges of patient-centred outcome research in RDs. Promotion of implementation of PCOMs in RDs contexts, i.e. clinical trials, clinical research and patient registries is hampered by the insufficient number of validated tools developed for RDs. This is demonstrated in the analysis performed by the ERICA Consortium where only less than 4% of RDs were found to be specifically addressed by one or several PROMs. To partially standardize PROM development and leverage synergies across RDs, ERICA WP3 leaders, ORPHANET and ICS-VHIR, in collaboration with the MAPI Research Trust have generated a PROMs repository of validated tools in RDs that are currently being linked to functions and disabilities in the International Classification of Functioning, Disability and Health (ICF). This preliminary work will allow us to directly match the ICF-coded core impact sets we will develop in T10.1 for each use case to suitable PROM items, thereby greatly facilitating the process of PROM scale generation and COA validation. Collection and integration of PCOMs, mainly PROMs data in T10.2 to improve patients' care pathways in RDs, improve monitoring of patients' health status, optimize clinical therapy guidance and ultimately improved health outcomes requires data standardization and efficient, regulatory-grade data capture. To leverage the full power of these PROMs datasets, they will be integrated with other COAs, mainly candidates for biomarkers via interaction with WP9, paving the way for personalised medicine in RDs. Overall process from regulatory and ethical clearance management, adaptation of existing mHealth or development of new ones, data standardization in CDM (OMOP) and integration with clinical data and OMICS data for further analysis through ML approaches will be designed and validated through 4 use cases involving the collection of patient-generated data using mobile health solutions and devices.

Objectives

The main aim of this WP is to promote the development and integration of PCOMs (PROMs and other types of COAs) together with PREMs and socioeconomic information for monitoring clinical research (clinical trials, clinical studies, patient registries, natural history studies) and assess its efficacy and safety for patients together with the evaluation of disease progression (symptoms, biomarkers etc). Towards this aim we will achieve the following specific objectives:

- To develop a platform for the development and validation of regulatory-grade PCOMs for RD, which are suitable for establishing truly patient-centred clinical trial endpoints, based on core disease/group of diseases impact sets on the patient as well as societal level.
- To develop and implement digital tools allowing efficient and broad collection of PCOMs patient self-reported data (PROMs/PREMs, socio-economic information) in RD patient cohorts and integration with patient databases and research data.

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- To systematically explore the societal impact and personal burden of RDs across Europe.

During Year 1 of ERDERA, WP10 specific objectives are:

- To establish the overall regulatory strategy for development and validation of PCOMs in RDs in T10.1, as well as for collection of data in T10.2
- To start defining the ICF core impact sets for the target diseases in T10.1
- To develop the study protocols for targeted use cases in T10.2 including selection of PROMs, and end-user requirements both clinical and technological.
- To identify available mHealth and devices and their readiness for adoption in T10.2

Description of Programmed Activities

T10.1. Platform for regulatory-grade patient-centred COA development and validation (M1-M12)
TL: UKHD; Contributors: VHIR, LMU, KUM, UT, APHP, Erasmus MC, MRT, EURORDIS. T10.1. aligns with GO:2,3; SO:1-4; OO:1,4,5.
In a multistakeholder patient-centred process, we will develop patient-reported outcome assessments and assess patient-relevance of top-ranked COA candidates for five demonstrator RDs (HSP/ataxia [ERN-RND], RASopathies [ERN-ITHACA], mitochondrial disease [5 ERNs], rare anaemia disorders [ERN-EuroBloodNet], and craniofacial anomalies [ERN CRANIO]. We will i) establish ICF-coded core impact sets for each of the RDs, ii) match ICF-coded functional impacts with suitable existing PROMs (Coll ERICA), and iii) validate PROMs in at least 3 European languages, establishing sensitivity to change, meaningful within-patient change and cross-language equivalence. Additionally, anchoring studies for top-ranked COA candidates in the four demonstrator diseases will be performed to establish their patient-relevance. **In Year 1,** T10.1. will develop an overall regulatory strategy and initiate establishing ICF core impact sets for each of our paradigmatic target diseases:

- In close collaboration with WP18 we will develop an overall strategy for development and validation of regulatory-grade PCOMs for each of the five paradigmatic demonstrator RDs that considers the unique challenges, requirements, and current status for each of the diseases.
- Establish a strategy to collect patient input on patient-relevant health aspects for each of the target diseases. Depending on the specific disease this process may include (semi-)structured interviews, focus groups and/or surveys and will ensure that we capture representative input not only in terms of disease stages or expression but also geographic, cultural, and socioeconomic background. Strategy development will be co-led by the respective disease-specific patient advocacy organisation (PAO) partners.
- In a PAO-co-led process we will design the content for respective input method, considering language barriers (see 2.: interviews, focus groups, surveys)), pilot test the methodology in small groups of patients and adapt as necessary.
- Lead a consensus process for each disease group to select a minimum of two COAs per disease group for further validation and anchoring studies to patient-relevant concepts of interest. CAOs will be selected based on their validation status and their demonstrated ability to detect longitudinal or treatment-induced change.

T10.2. Development and Implementation of Clinical Outcome Assessment Tools (M1-M12) *TL: VHIR; Contributors: UT, APHP, UKHD, UPM, EURORDIS.* T10.2. aligns with GO:2,3; SO:1-4; OO:1,2,5.
In this task methodologies to develop and implement digital tools e.g. mobile health solutions (mHealth) to collect PCOMs (i.e. PROMs/ObsROs/PerfOs, socio-economic, lifestyle data) linked to clinical data in the EHR and patient registries and research data will be developed. Methodologies will be validated through four case studies collecting PCOMs using mHealth solutions and devices. They case studies have been selected representing a wide range of RDs; PROMs/QoL data collected through a mHealth (1) ERN EpiCARE (APHP) linked to the EURO-NMD registry and (2) ERKNet

(UKHD) linked to the ERKReg registry; (3) PROMs, patient reported health forms, socio-economic and nutritional information collected through a mHealth and integrated with clinical and research data for ERN-EuroBloodNet linked to RADeep registry (Rare Anaemia Disorders European Epidemiological platform) (ICS-VHIR). A (4) case study will combine real-life sensor-based mobility performance capture with activity-triggered real-life patient-experience sampling (ERN-RND/UT) and combine these datasets with the ARCA Registry (Autosomal Recessive Cerebellar Ataxia registry). **In Year 1, we will initiate most of the tasks foreseen in Phase I: Co-design and development:**

- Development of the study protocols for the 4 case studies including the collection of end-users (i.e. patients and researchers) clinical and technical requirements. This will be done in collaboration with WP9 to integrate PCOMs data with other type of data collected in WP9 such as clinical data in the EHR T9.1, natural history studies T9.3 and COAs for disease progression T9.5. The study protocol will also include the selection of validated tools for PROMs/ObsROs collections based on available instruments in the public repository created in ERICA. Technical requirements will be discussed with WP13 for alignment with the Data Services hub under T13.1. Steering of the Data Services Hub (DSH) and the RD-VP.
- Identification of available mHealth (e.g. NORA (stroke), KIWAME (hydratation)) and devices and their readiness for adoption or implementation as well as need for development of new mHealth solutions. A first workshop will be organized between clinical partners and IT partners in WP14 to identify the technical requirements for integration of PCOMs information with data in EHRs and registries as well as research data. Initial plan for data readiness and FAIRification will be developed with the support of the DataHub in WP14, T14.1. Services for making data findable, accessible, interoperable, reusable for automated applications.
- Clarification of regulatory aspects: mHealth privacy and security protections, EU/national - regulatory approval processes. Regulatory aspects related to mHealth solutions adopted or newly developed in the use cases will be assessed in the context of the applicable EU and national regulations for medical devices. An initial plan for regulatory clearance for mHealth-derived data in clinical research will be developed with the support of WP18, T18.2 Regulatory support to clinical research.

T10.3. Unveiling the Hidden Burden: Estimating the Socioeconomic Impact of RDs for Informed Decision Making and Resource Allocation (starts M13) *TL: Sciensano; Contributors: Erasmus MC, RDI, EURORDIS, APHP, WDO, CVBF, QUB-UK**. T10.3. aligns with GO:2,3; SO:3,4; OO:1,4,5.
The main aim of this WP is to promote the development and integration of PCOMs (PROMs and other COA types) together with PREMs and socioeconomic information for monitoring clinical research (clinical trials, clinical studies, patient registries, natural history studies) and assess its efficacy and safety for patients together with the evaluation of disease progression (symptoms, biomarkers etc.).

Additional deliverables *(additional to those included in part B of the proposal)*

D10.1: Design of respective input method (structured interview, focus group, survey) completed and pilot tested (M12).
D10.1: Top-ranked CAOs for further validation selected for each target disease (M12).
D10.1: Regulatory strategy for each target disease established (M12).

Set of Activities Number	**11**	**Start Date or Starting Event**	**M1: September 2024**
Set of Activities Title	**Innovative Therapies - ATMPs**		

Short name of participant& (No)	UKHD (13)	EURORDIS (26)	CVBF (50)	FTELE (5)	Pfizer* (161)
Person Months	9	9	3	12	
Start month	M1		**End month**	M12	

**Associated partners providing in-kind contributions*

State of the art behind this WP

One of the most critical limitations existing toward developing ATMPs based on gene therapy for RDs is the absence of a clear and straightforward path to the clinic. This is not only due to the complexities associated with the technologies involved but also the specificities associated with their use in RDs. WP11 will create a strong network of clinicians and experts in ATMPs development with the aim of simplifying the procedures for the selection of RDs with the highest potential for treatment and for the identification of the technologies more adapted to be translated to the clinic for the defined disease.

Methodology

WP11 will streamline the development of Adeno-Associated Virus (AAV) and mRNA technologies aiming to increase the speed and reduce the costs associated to the clinical translation with these technologies. WP11 will instead focus on the creation of a collection of procedures and methods to identify diseases ranked based on medical needs, match them with technologies suitable for clinical translation and simplify the procedures to access clinical trials. The objective is also to provide proof-of-concept of gene transfer with the chosen technology in multiple diseases with a common preclinical strategy as defined by the main actors of gene therapy in Europe. This WP will coordinate efforts with the accelerator hub and WP12 also working on the clinical translation of the ASO technology for RDs. These continuous interactions between the three WPs, also ensured by the participation of key members of this WP in the two others, will be key to identifying a common and efficient strategy to perform clinical trials in RDs.

The work of this WP is divided temporally, with the first three years that will be dedicated to the diseases prioritization and matching with the technologies identified and streamlined in the accelerator hub. The last four years will be dedicated to the generation of the proof-of-concept studies and the preparation of the clinical trial application for a start at the end of year seven of the project.

Objectives

This WP aims to demonstrate the applications of established innovative, scalable technology platforms of ATMPs developed in the Acceleration hub for prioritized RDs. This WP will collaborate with the two WPs that focus on diagnosis and natural history studies, which are essential for therapy development. **In Year 1**, the objective will be to identify the most urgent and suitable disease groups for ATMP therapies.

Description of Programmed Activities

T11.1. Identify and rank disease indications requiring ATMPs (M1-M12) *TL: UKHD; Contributors: EURORDIS, CVBF.* T11.1. aligns with GO:2; SO:1,2,4,5.
This task will serve to identify, prioritize, and select in an unbiased manner RDs and conditions with the greatest need and best suitability for the development of innovative ATMP therapies. To this end, **in Year 1**, a scoping review and a multistakeholder survey involving clinicians and scientists from all ERNs, patient organizations (including the WP1 PPIE core group), translational researchers, HTA experts and social scientists will be performed across ERDERA. This task will take into consideration the work already performed in this area in the context of the EU-funded project ReSTORE; the RAREIMPACT initiative, the TRANSORM Alliance as well as by benchmarking current initiatives such as the UK CATAPULT Cell and Gene Therapy.

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Both the scoping review and the multistakeholder survey will be completed by M12. The evaluation and exploitation of the review and survey results will be performed in the first half of year 2. In a first step, general criteria for ATMP treatment suitability will be pre-defined by ATMP experts to inform the selection process (by M6). The main parameters and their relative weight in the decisional algorithm will include the disease demographics, morbidity/disability, potential for therapeutic efficacy based on mechanistic considerations, availability of established intervention endpoints, availability of natural history studies, efficacy and safety of currently available therapies, availability of European study cohorts based on registry information. From the collected information available and analysed by M18, priority lists of suitable candidate conditions with the greatest anticipated potential benefit from ATMP therapies will be derived for each ATMP class and the most promising candidates will be chosen for demonstrator projects.

T11.2. Select and adapt the technical platforms with prioritised need (starts M12) *TL: GNT; Contributors: INSERM_ART-ARNm, Pfizer*.* T11.2. aligns with GO:2; SO:1,4; OO:2.

T11.3. Design the proof-of-concept studies to evaluate the selected pipelines (starts M36) *TL: INSERM_ART-ARNm, INSERM_IT-GGB; Contributors: GNT, FHG.* T11.3. aligns with GO:2; SO:1,4; OO:2.

T11.4. Evaluate the selected platforms for CTs requirement and joint transnational call (starts M48) *Contributors: CVBF, UC, GNT, INSERM_ART-ARNm.* T11.4. aligns with GO:2; SO:1,4; OO:2,3.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**12**	**Start Date or Starting Event**		**M1: September 2024**
Set of Activities Title	**Innovative Therapies - N-of-Few Approach**			
Short name of participant & (No)	LUMC (16)	UT (8)	UKHD (13)	RCC* (162)
Person Months	6	12	12	
Start month	M1	**End month**		M12

**Associated partner providing in-kind contribution*

State of the art behind this WP

About 70% of RDs are of genetic origin. For these patients, gene and genetic therapies could have therapeutic effects. However, many patients suffer from ultrarare diseases and for genetic therapies mutation specific approaches are often required, which apply to very small group and sometimes even individual cases. So, on the one hand, these individuals are very eligible candidates for genetic or gene therapy treatment, but on the other hand due to the small number of cases, there is no commercial interest to develop them. Notably, it has been shown possible to develop individualized antisense oligonucleotides (ASOs) within an academic setting in the USA (1). Similar developments are starting in Europe (2,3,4). However, due to the individualized nature of the treatment, the traditional drug development pathways and processes do not apply and in Europe individualized treatment can be done under a named patient setting, without the goal of marketing authorization. This offers more flexibility than traditional drug development, but currently there is no consensus on processes and steps involved. To ensure safe, standardized and timely development of individualized treatments a new platform has

to be generated to. This will work towards the IRDiRC goals of having 1000 affordable therapies by 2027 and will address the current unmet medical need of patients with ultrarare diseases.[7,8,9]

Methodology

Various aspects of the platform will be elaborated in M36 utilizing the genuine expertise in N-of-1/N-of-few ASO treatments of the leaders of this WP (Aartsma-Rus preclinically, Synofzik clinically), making sure to align with WP13 (virtual platform) with regards to ontology and usability. It is anticipated that the work done in WP7 and WP8 will identify additional patients with mutations eligible for individualized ASO treatment. The individualized treatment platform will be developed by the core partners in M1-M36, and rolled out to other partners via the hub and spoke model, where some aspects will be coordinated by the core partners (LUMC, UT)(patient identification, ASO design and synthesis, safety assessment in cells and animals and ethics), while other aspects will be implemented at the sites treating patients with individualized therapies (selecting relevant outcomes, design the study/treatment regimen, local regulatory aspects and challenges for local treatment implementation). Rolling out to other partners will be initiated from M1, where a patient with ataxia telangiectasis has been identified who carries the same mutation as a patient currently treated with an ASO in an individualized setting in UT. For this work we will be able to draw on already existing first emergent cross-European networking efforts by the two TLs, (LUMC, UT, both coordinators of 1 mutation 1 medicine, 1M1M) both at the preclinical and clinical implementation level, including also already first contacts to underrepresented countries (via ERN-RND and linking to WP24).

As there is currently no platform to facilitate individualized treatments, we expect that optimization of the first 'build' of the platform is required. We will test the interoperability of the different aspects of the platform and how each aspect functions with 4 use cases. The first 2 use cases are ASO specific selected cases from UT (Ataxia Telangiectasia) and UKHD (POLR3A-related neurodegeneration) and will be run in stage 1. These use cases will identify potential bottlenecks or suboptimal functioning of aspects of the platform that need work. In stage 2, 2 additional use cases will be selected (treatment modality and disease to be determined, ASO or ATMP). These use cases will be selected to specifically assess bottlenecks identified in use case 1 and 2, are solved.

Individualized treatments check for eligibility based on mutation type, rather than disease. This is a paradigm shift from normal drug development. To ensure identification of eligible mutations, this WP critically relies on interaction with other parts of the ERDERA. Collaboration with CRN – Diagnostic Research will allow us to first identify patients eligible for individualized ASO treatment and later will benefit from the algorithm developed in this WP that will automatically flag patients potentially treatable in the ERN registry.

To ensure equity and selection of the most eligible patients, we will establish a treatment board, which is a multidisciplinary group of experts who will discuss eligibility of the patient for individualized treatment based on mutation, disease and patient-specific aspects, which outcome measures to select. The treatment board will have representation from patient groups, clinicians, researchers and ethicists. The treatment board members will be recruited from relevant experts in the CRN and the Expertise Services Hub (WP17, 18 and 19). Detecting treatment effects will rely on outcome measures and n-of-1/n-of-few progression and treatment response modelling, and therefore facilitated by CRN – Outcome Research and WP 19 Methodological Support, to fit the n-of-1/n-of-few setting, such as real-world outcomes and progression modelling, CRN-Outcome Research; identification of a toolbox of disease-specific and generic outcomes.

Patients will be treated in a named patient setting, but to facilitate drawing general conclusions, and through the collaborative work with WP19, it will allow assessing the efficacy of the platform approach across diseases and treatments. Which clinical treatment centres will be qualified first will depend on the location of eligible patients. However, the centres will be selected from partners of the ERDERA. Individualized treatment has unique regulatory and ethical challenges. However, our discussions will benefit from ongoing efforts on these aspects in the ERDERA Expertise Services Hub) and the EAG.

Treatment response will be captured in a specific registry, that has the flexibility to be individualized for each patient. Outcome measures will be selected by the clinician and patient/family and natural history captured before and after treatment. The registry will be built with support of WP13, WP14, and WP 15.

Objectives

The objectives for the Year 1 are the following:

- Start working on all aspects of the platform.
- Consensus on patient identification criteria.
- Brainstorm on selecting outcome measures, trial design and treatment site criteria for N-of-1 treatments.

Description of Programmed Activities

The goal of WP12 is to establish an innovative, scalable platform for academic development and implementation of mutation-specific antisense oligonucleotide (ASO) treatments for individuals with nano-rare RD mutations. Along this pipeline we will create a combined preclinical/clinical/regulatory framework for tailored N-of-1/N-of-few treatments; and implement, standardize, and optimize each of its modules, processes and levels. The pipeline will be built through a multistakeholder collaboration effort, where we will actively include underrepresented countries in generating guidelines and processes. For this platform every aspect will have to be individualized, the ASO treatment, but also the outcome measures will have to be selected to measure relevant benefit for each patient, consent will have to be customized. Furthermore, patients will ideally be treated in the hospital where they receive expert care. This means implementation of N-of-1 treatment locally in multiple hospitals.

T12.1. Academic platform development (M1-M12) *TL: LUMC; Contributors: UKHD, UT, SRUMC, UKLFR,WDO, RCC*.* T12.1. aligns with GO:1; SO:1; OO:3,5.
To establish an innovative, scalable platform for academic development and implementation of mutation-specific antisense oligonucleotide (ASO) treatments for individuals with nano-rare RD mutations. Note that patients will be treated in a named patient, experimental treatment setting. As such, regulatory advice for processes is foreseen, but the regulatory approval is not mandatory. Furthermore, while each development is individualized, processes and steps are similar. To ensure development in a standardized, safe, and timely fashion we will create a combined preclinical/clinical/regulatory framework for tailored n-of-1/n-of-few treatments; and implement, standardize, and optimize each of its modules, processes, and levels. The platform will cover the following aspects:

- Identification of patients with mutations eligible for individualized ASO treatment (link to diagnostic registries in ERNs) and establishing eligibility criteria based on mutation, disease and patient and establish an independent treatment board to discuss eligibility) (link to ethics T1.6)
- ASO design and synthesis (consensus on quality criteria for GMP-like production and optimizing methods for smaller scale production required for individualized treatments, done by experts in ASO synthesis, discussion with local regulatory bodies, link to WP18 Regulatory Support)
- Efficacy assessment (consensus on processes developed by LUMC, UKHD, SRUMC and UT)
- Toxicity and safety assessment (consensus on process and reducing the need of animals by LUMC and SRUMC, input from WP18)
- Identification of patient relevant outcomes in an N-of-few setting and run-in natural history studies to establish the trajectory before treatment (during development of the individualized therapy) vs after treatment (T12.2)
- Consensus on intervention strategy and assessment of treatment effect (benefit and side effects) (T12.3)

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- A registry to capture individualized patient relevant efficacy and safety outcomes before and after treatment (link to WP13, 14 and 17, coordinated by UKHD & UKLFR)
- Implementation of first in human treatment infrastructure in N-of-few setting (T12.4)
- Regulatory aspects (while we do not need regulatory approval, we value advise, link to regulatory WP18 and Expertise Services Hub)
- Ethical framework (ethical aspects are involved in many steps and processes, link to T1.6)

Specific plan for Year 1 of T12.1 includes:

- Patient identification: when considering patients, eligibility should be assessed based on objectives measures. These involve the mutation (eligibility), the diseases (progressive, likely to respond to treatment) and the patient themselves (expected benefit, local treatment possible, start and stop criteria, informed consent etc). To ensure that the criteria are discussed properly a treatment board will be set up including multistakeholder representatives (geneticists, clinicians, patient representatives, ethicists, regulators) and processes for standardized assessment will be generated. Towards setting up the treatment board and establishing eligibility criteria, a consensus meeting will be organized (M12) involving different stakeholders from the network and including at least 25% of participants from underrepresented countries.
- ASO design and synthesis: there are currently no processes for GMP grade production of small scales, as needed in individualized treatment. Towards preparing for a consensus meeting in Year 2, **in Year 1 protocols will be compared and zoom meetings with manufacturers and experts in quality assessment will be held.**
- Efficacy assessment: to measure efficacy of the treatment outcome measures that measure something that is relevant to patients and reflects an aspect that is expected to respond to treatment are required. Given that treatment is individualized, these outcome measures need to be individualized as well. To facilitate selection of responsive measures for which protocols are available a toolkit of outcome measures will be prepared. **In Year 1,** in preparation for a consensus meeting in Year 2, **online meetings will be held in Year 1 to compare protocols for initial alignment and a list of outcome measures to consider.**
- Toxicity and safety assessment: currently each ASO has to be tested in in vivo toxicity studies. Ideally these are replaced by in vitro studies to reduce the number of animals. **In Year 1**, research will be initiated on in vitro models to assess toxicity with ASOs known to be toxic in humans but safe in rat toxicity studies to elucidate which in vitro studies predict in vivo toxicity.
- Individualized treatment effect capture registry: as this involves individualized treatment, there will not be a control group, but rather data from before and after treatment. This will require a registry that allows capturing this and that is adaptable to the N-of-1 treatment aspects (different ASOs for different diseases rather than a compound or disease specific registry): **no activity in Year 1.** This will require a registry that allows capturing this and that is adaptable to the N-of-1 treatment aspects (different ASOs for different diseases rather than a compound or disease specific registry). **No activity is planned in Year 1.**
- Regulatory: N-of-1 treatment with ASOs is given as an experimental treatment and as such qualifies as patient care, rather than a clinical trial. There is no objective to file for marketing authorization and regulatory approval is not the goal. Still regulatory advice is pursued and exploratory zoom calls with regulatory experts in the network to discuss the peculiarities of N-of-few.
- Ethics: the individualized treatment approach involves many ethical aspects. Rather than discussing them in an ethics focused meeting, they will be part of consensus meetings organized by the WP. **For the meetings organized in Year 1 for this and following tasks, pertinent issues will be discussed as scientific publications to share with the wider community (anticipated in Year 2).** For the meetings organized in Year 1 for this and following tasks, pertinent issues will be discussed as scientific publications to share with the wider community (anticipated in Year 2).

T12.2. Identification of patient relevant-outcomes (n-of-1/few) and run in natural history study (M1-M12) *TL: UT; Contributors: UKHD, LUMC, FSJD-CERCA.* T12.2. aligns with GO:2; SO:1; OO:3,5.
Develop adapted processes for patient-relevant outcome selection (CRN – Outcome Research) to fit the N-of-1/N-of-few setting; identification of a toolbox of disease-specific and generic outcomes coordinated by the WP manager during consensus meetings that involve multiple stakeholders from across Europe (with a focus on underrepresented countries), including patients; for each individualized treatment, the outcome measure will be selected by the patient/family and the clinician from the toolkit and then implemented in a natural history studies to determine individual sensitivity to change of candidate outcomes and pre-treatment progression trajectories.

Plan for Year 1 for T12.2: Identification of patient relevant outcomes in an n-of-few setting and run-in natural history studies (see aspect 3 of T12.1): plan and conduct a brainstorm meeting with experts to select candidate outcome measures (M10) (jointly with T12.3). **Plan for Year 1 for T12.2:** Identification of patient relevant outcomes in an N-of-few setting and run-in natural history studies (see aspect 3 of T12.1): plan and conduct a brainstorm meeting with experts to select candidate outcome measures (M10) (jointly with T12.3). Ethical issues will be discussed as well.

T12.3. Treatment/study design and analysis (M1-M12) *TL: UT; Contributors: UKHD, UKLFR, LUMC.* T12.3. aligns with GO:2; SO:1; OO:3,5.
Individualized therapies are provided as experimental treatments, rather than tested in a clinical trial setting. Still, ways to assess therapy effects are required for patient management. Here we will achieve consensus on strategies to evaluate treatment efficacy on an N-of-1 level (e.g., implementation of staged evaluation milestones: safety – target engagement – efficacy on surrogate parameters – clinical efficacy). A consensus will be achieved via stakeholder meetings that include participants from across Europe, with a focus on underrepresented countries.

Specific plan for Year 1 for T12.3. includes: Treatment/study design and analysis: the challenge with individualized treatment is that rather than a control group, there will be trajectories before and after treatment. This will require specific study design and statistics. Toward this, a brainstorm meeting with experts to discuss study design and analysis will be planned in M10 (jointly with T12.2)

T12.4. Implementation of first in human treatment infrastructure (M1-12) *TL: UKHD; Contributors: UT, LUMC.* T12.4. aligns with GO:2; SO:1; OO:3,5.
Development of criteria and a process for site qualification; establishment of a network of qualified clinical sites in major European countries that can carry out N-of-1 treatments (i.e., not the same as running a clinical trial). Based on the feedback and during consensus meetings the procedure will be optimized further. The processes will be coordinated by the WP manager.

Specific plan for Year 1 for T12.4 includes: To avoid patient burden, the goal is that patients receive individualized treatments in the centres where they receive expert care. There are requirements to allow individualized treatment in the centres where patients receive expert care that have to be in place in all centres, but there will also be country and centre specific requirements.

T12.5. Case studies (starts M13) *TL: UT, UKHD; Contributor: LUMC.* T12.5. aligns with GO:2; SO:5; OO:1,3.
The power of the platform generated in T12.1 will be shown by 4 use cases, selected to represent different challenging scenarios (e.g. N-of-1; N-of-few; childhood/adult onset; target tissue e.g. brain/eye/liver) to pressure test the platform. We will start with 2 use cases using ASOs for ataxia telangiectasia and POLR3A-related neurodegeneration in M13-36. In M50-M84, 2 other use cases will be selected from within the network (e.g. Acceleration Hub). These use cases can be ASOs (using the whole platform) but also ATMPs, where the ASO specific pieces of the platform will not be used. Selection will be facilitated by the selection criteria set in the treatment board (T12.1), and we will

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collaborate with WP21 for eligible individualized ATMP candidate use cases. Note that for each use case a contribution towards development costs will be provided.
No activities are planned for Year 1.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**13**		**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Rare Disease Virtual Platform (RD-VP) finding and accessing the data ecosystem**						
Short name of participant & (No)	INSERM_ Orphanet (1)	UTWENTE (17)	LUMC (16)	UPM (18)	UMCG (19)	AIT (36)	BBMRI-ERIC (132)
Person Months	8.62	13.28	10.39	10.71	10.71	6.25	2.82
Short name of participant & (No)	GUF (66)	ULEIC* (171)	AUMC (20)	SRUMC (11)	Pfizer* (160)	ROCHE* (164)	
Person Months	3.73	1.43	6.14	5.2	0.33	0.33	
Start month	M1			**End month**	M12		

**Associated partners providing in-kind contribution*

State of the art behind this WP

With over 6,000 RDs, most of them affecting less than one person in a million across the globe, covering all areas in medicine, rarity constitutes the major bottleneck to conduct effective and efficient research, and one of the reasons for that is the difficulty in identifying, collecting, harmonizing and integrating the critical mass of data that is necessary to understand RD, improve their diagnosis, and develop therapies and strategies to improve patients' lives. Following the Rare2030 vision, the majority of PLWRD will have their data integrated to a federated health and research data ecosystem. The data challenge in fostering RD research is to get a diversity of types of data reusable in a timely

manner. Tackling this diversity and heterogeneity needs a constant effort towards interoperability amongst data sources and towards federation in an ecosystem that allows researchers, and the algorithms that work for them, to find and use the data that they need in advanced automated analysis rapidly and easily. In addition, the ecosystem should provide mechanisms to transform the results of research into reusable knowledge by exploiting reference data (knowledge bases) and improving them for future research. Data acquisition, analysis, transformation, and reuse constitute the pillars of a virtuous cycle of data optimisation for better RD research. Importantly, applying these mechanisms multiplies the value of RD data for Bonafide analysis at a global scale delivering the ERDERA Data Hub (ERDERA-DH) as value proposition.

All ERDERA projects that manage data are expected to contribute to the ERDERA-DH. The contributing project will benefit, but a test case for ERDERA as a partnership is that stakeholders outside of an individual CRN, JTC, or CT project benefit from the ERDERA-DH. The role of the Data Services Hub is to enable partners running projects within the ERDERA to deliver the ERDERA-DH. Importantly, it will develop mechanisms to increase the value-adding capacity of ERDERA partnership substantially. The volume and breadth of types of data and analyses that must constitute the ERDERA-DH far exceeds that of previous projects.

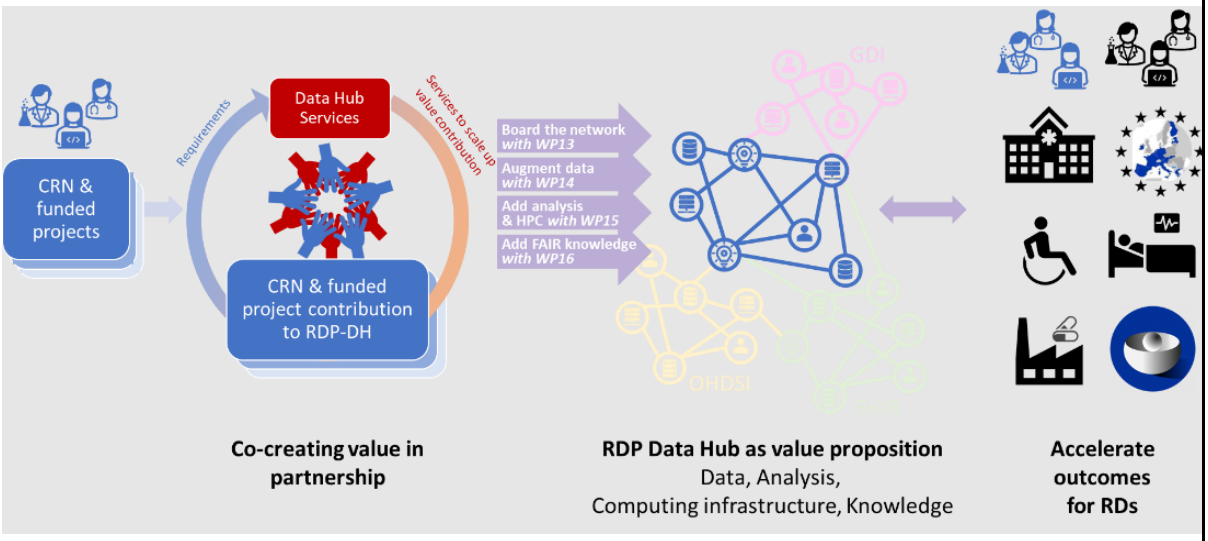


Figure 10. Co-creating the ERDERA Data Hub as value proposition.

The Data Services Hub brings together, and leverages on, the outputs of projects and initiatives that contribute to the global data strategy:

- EJP RD virtual platform that developed a set of standardised methods and tools to create a federated network of resources relevant for RD research that are findable, accessible, interoperable, and reusable also in automated scenarios (conform to FAIR principles), and generated reference data (RD workflows and networks) based on system biology approaches;
- Solve-RD that set up methodologies and pipelines to foster genetic RD diagnosis and developed a database of treatable RD variants (the Treatabolome);
- ERICA that created the first RD specific PCOMs repository based on a standard methodology to code patient-centred instruments to measure functional impacts of RD;
- Orphanet, the knowledge base specific for RD, produces ontologies centred on the ORPHAcodes, and provides a corpus of reference genetic, epidemiological, functional and phenotypic data for RD research.

State of the art behind the WP13

The RD Virtual Platform (RD-VP) is a network of resources and data sources able to interoperate with each other by the adoption of a set of semantic and technical standards that increase their readiness for

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RD research. Resources in the VP network can be found and queried in a federated manner through entry points such as the VP Portal, that is a reference implementation for other stand-alone or plug-in entry points. Examples are VP wide analysis functions incorporated in ERN web sites, Jupyter notebooks for bioinformatics analysis, or resources that which to extend their data exploration environment with RD resources. This ecosystem has been built during the EJP RD (2019-2024) and will scale up in ERDERA for the network to be enlarged to new resources, and eventually other VP-compliant thematic networks, and the resources' content to be more deeply queryable and reusable for RD research projects funded in ERDERA through Joint Transnational Calls (JTCs), clinical trials (CT) or within the CRN.

Methodology

Methodology behind the Workstream 'Data Services Hub'

Vision: The DSH is an integrated, evolving, set of methods, services, tools, and reference knowledge bases usable by the RD multi-stakeholder's community to perform more efficient research by facilitating the capture, collection, and reuse of data. The DSH, as the ERDERA data infrastructure, is a central component of the ERDERA value proposition. To achieve this vision, the DSH is developing and providing scalable and sustainable solutions to the case studies in CRN and JTCs funded projects and clinical trials (CT), as means to demonstrate the usefulness of the DSH for RD research.

The mission of the DSH is to develop and provide scalable and sustainable solutions to the case studies proposed in CRN and JTCs, as means to demonstrate the usefulness of the DSH for RD research, by creating a virtuous cycle from the harmonization, collection, integration, analysis, and reuse of data in a diversity of contexts. In other words, by taking the ERDERA case studies as exemplars of the RD research community needs, the DSH aims at tackling the scalability and the sustainability challenges of a data infrastructure in the RD research field.

While the EJP RD has developed the federated infrastructure for RD research data, namely the Virtual Platform (VP), by adopting a set of standards, both semantic and technical, methodologies and facilities to find and access data for RD researchers, the DSH will scale up the VP thanks to the widening of the case studies provided by the CRN and the JTC funded projects and CTs, which will trigger the development or the refinement of a set of services and tools, which in turn will be integrated in the ecosystem for future reuse. The whole DSH is designed as a virtuous cycle that can be triggered at any stage by each of the case studies or projects in the ERDERA. WP13 will streamline the demands arising from CRN or JTC-funded projects/CTs case studies to the appropriate DSH WP and ensure the integration of other WPs' outputs in the federated VP infrastructure, assessing and ensuring their compliance to the ecosystem requirements, in particular their FAIRness and their findability by the community through a VP Portal. WP14 will provide ERDERA researchers with methodologies and tools to capture their data more easily in compliance with the RD adopted standards and optimized for the specific aim for which they are collected, while WP15 will provide methods, tools and infrastructure to deposit, share and analyse a diversity of data, with a special attention to the reusability of results, in compliance with the VP requirements. Building on pre-existent knowledge resources, WP16 will develop them further and integrate together around RD maps, guided from ERDERA case studies, and capturing the reference knowledge produced by them. As part of its strategy, the DSH will interact with other data infrastructures and initiatives as far as they stimulate DSH developments and provide re-usable solutions to it.

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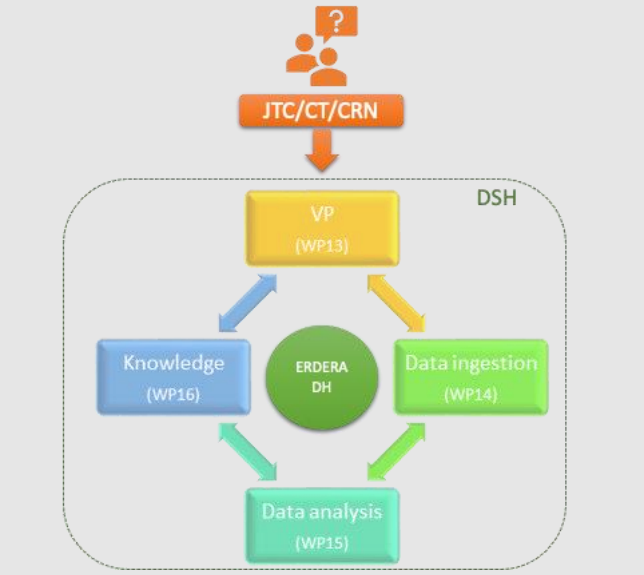


Figure 11. The Data Services Hub workflow towards the ERDERA Data Hub as a value proposition

The Data Services Hub will provide consistent methods, tools and services embedded in a data ecosystem, that are standardized and scalable. Seeking scalability and sustainability needs a stepwise approach designed by tracking back from full delivery in Year 7, through Year 3 as a major milestone and Year 1 as a baseline. Indeed, to ensure alignment across tasks in the WPs, across WPs within the workstreams, and across other workstreams, it is crucial to lay out a workflow that helps establish the interactions to provide specifications, proofs-of-concept, and the end results. **Year 1** will specify the requirements that need to be fulfilled to provide solutions to other workstreams' case studies. This needs to be aligned across all DSH WPs with WP13, to ensure we establish a well-aligned infrastructure of tools and services. By Year 3 we will demonstrate feasibility and scalability of service provision by delivering proof-of-concept solutions for most or all of the case studies taken. These solutions will be scaled up to full delivery by the end of the 7-year-project.

The Data Services Hub considers the following requirements for AI approaches:

- Technically robust, accurate and reproducible, and able to deal with and inform about possible failures, inaccuracies, and errors, proportionate to the assessed risk they pose. The approach in the ERDERA DSH, will be robust and accurate in the sense of providing the adequate levels of quality in the processes, and reproducible since techniques used will be documented properly in the deliverables. As well failures and inaccuracies will be minimized in the DSH as those techniques dealing with data, for instance in FAIRification processes which involve suggesting ontology-based annotations for data elements and values, will be validated by data stewards. The performance of this hybrid intelligence will be assessed and compared to that of a purely manual approach to minimize annotation errors and bias. Another element is in the support for the analysis with AI in WP15. AI training and analysis will be implemented as a distributed AI support in a federated manner. This can easily scale-up and be reproducible in the data nodes of the ERDERA federation.
- Socially robust, in that they duly consider the context and environment in which they operate. The techniques to be used with AI within the DSH will be in cooperation with other tasks of the project (e.g., WP6, 9, 10) where AI models will be used in the studies of different diseases involving patients' data. The social acceptance and context will be a part of the design of the DSH requirements in WP13, and the operation environment oriented to the use of the results by health professionals and health researchers.
- Reliable and function as intended, minimizing unintentional and unexpected harm, preventing unacceptable harm, and safeguarding the physical and mental integrity of humans. The application of AI will be reliable and avoiding the potential risks of harming even

unintentionally. As commented, for FAIRification data processed, annotations for data elements and values, are validated by data stewards. We will safeguard the potential misuse of the processes with a human validation, providing human friendly tools for such purpose for the data stewards.

- Able to provide a suitable explanation of their decision-making processes, whenever they can have a significant impact on people's lives. Data integration and FAIRification of data involve different processes which imply data transformation, homogenization and other processes which can be supported using AI methods. The methods which will be used (knowledge graphs, pathway-level interpretations, ontology-based methods, or neural networks-based methods among others) will be provided with the required level of explainability and "interpretability" of the decisions suggested, discarding methods which are not able to provide the sufficient level of explanation with the current available techniques (e.g., SHAP, LIME, etc.).

Definitions:
The ERDERA Data Hub as value proposition, or the 'ERDERA Data Hub' (ERDERA-DH): an integrated network of Findable, Accessible, Interoperable, and Reusable sources of data and other materials, analysis methods, knowledge bases, and high-performance computing components that is collectively created by all partners in ERDERA. Integrating resources in a network and making them FAIR adds value to the resources, constituting a critical outcome of ERDERA. The services offered by the Data Services Hub facilitate a transformation of data, analysis, knowledge, and compute services for use by a wide range of stakeholders, including the original creators. The services are created in collaboration between ERDERA partners and the Data Services Hub.

- DSH methods: Set of procedures and workups provided to researchers and to resources and data sources holders to improve their integration into the VP ecosystem, the preparation of their data, the data sharing and analysis and the exploitation of reference knowledge resources. Ex: VP onboarding guidance.
- DSH tools: technical artifacts developed and provided within the DSH, together with their technical specifications. Ex. FAIR-in-a-Box; VP Beacon2 API specification.
- DSH services: a set of human or technical facilities for end-users to apply the DHS methods and/or implement the DSH tools. Ex: VP onboarding stewardship; VP query facilities; documentation and tutorials to 'do it yourself' purposes as a package.

Methodology behind the WP13
This WP focuses on the maintenance and evolution of the Rare Diseases Virtual Platform as the foundation for the ERDERA-DH. Here, we consider evolution both in the sense of expanding the number of participating resources (T13.3 – VP onboarding services) and in the sense of increasing the features, robustness, and resilience of the platform (T13.2 – RD-VP evolution and scaling-up). These evolutions are guided by the strategies defined by T13.1 – VP/Data Services Hub steering regarding new resources or resource types that should be included in the RD-VP. These new resources may have characteristics and requirements that either completely fit the RD-VP or require modifications and/or adjustments to the platform to be properly onboarded. Once needs for adjustments to the platform are identified, T13.2, which is responsible for the curation of the RD-VP's architecture, proceeds to evaluate the requirements and modify the RD-VP's architecture and implementation guidelines accordingly. These processes of identifying new resources to be connected to the platform and new functionality for the platform will be constant throughout the duration of the project. Main methodological principles in this WP are:

- Prioritization: Adapt and evolve the VP so that WP14, WP15 and WP16 can provide the services needed by CRN's projects to deliver, and to dynamically adapt the provision of services to JTC/CT funded researchers.
- Agility and continuous delivery: A robust and size-limited development team will work in agile cycles (sprints), T13.2 acting as Product owner and the CTO acting as scrum master.
- Interoperability and harmonization: For semantic and technical interoperability developed in EJP RD will be enforced to make use of the standard ontologies (in WP16) and to allow

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different technical standards to interact. The list of EJP RD selected standards will be used and updated during the ERDERA partnership.
- Traceability: Developments, models, specifications will be documented and versioned in a GitHub space.
- Quality: FAIR principles- and VP specifications compliance will be assessed.

Objectives

In **Year 1**, the objectives of WP13 are the following:
- To organise the workflow and to technically lead the teams of Data Services Hub and CRN/JTC/CT researchers and developers to ensure a perfect alignment of Data Services Hub activities from Year 1 onwards. Ultimately, to effectively complete projects that result in increasing numbers of stakeholders contributing to the Data Hub as value proposition (effectuate the CTO role).
- To support WP14-16 in their collaborations with projects contributing data, analysis, and knowledge to the ERDERA data hub as value proposition.
- To scale up the federated infrastructure built in EJP RD (RD-VP) by evolving a service-oriented architecture (SOA) to accommodate data, knowledge, and analysis methods from related CRN/JTC/CT projects.
- To onboard sets of resources, to make them automatically findable within the SOA-based ecosystem, accessible under well-defined conditions, interoperable based on the ecosystem's implementation guidelines, and reusable (allow for querying and reusing data within the connected resources).
- To continue or start the interactions with other ecosystems in Europe and at the international level as far as they respond to ERDERA needs.

Description of Programmed Activities

T13.1. VP/Data Service Hub steering (M1-M12) *TL: INSERM_Orphanet, LUMC ; Contributors: AUMC, UTWENTE, Pfizer*, ROCHE*. Data Services Hub Task leaders, CRNs WS leaders, Funding research WS leaders, National and international alignment WS leaders.* T13.1. aligns with GO:1-3; SO:1-5; OO:2.
Year 1 will focus on the creation of the Data Services Hub (DSH) procedures and workflows, to ensure cross-DSH alignment and integration in delivering a scalable and sustainable data service ecosystem based on the extension of the EJP RD Virtual Platform content and functionalities. The extension and evolution of the RD VP will follow a steering and prioritization process at the strategic level and an agile process at the operational level. By the end of **Year 1**, it will deliver a steering and prioritization model to drive a cost-efficient decision-making process on 1) methods that support scaling up the connection of new resources and 2) supporting new functionalities demonstrating added value of the ERDERA. The VP is expected to evolve into an intelligent learning system in which newly added resources contribute to statistical, AI, and machine learning applications. WP14-16 respectively guide addition by internal and external stakeholders of data resources (WP14), analysis methods and infrastructure (WP15), and knowledge bases (WP16). Each contributes new functionality that may trigger an update of VP specifications and onboarding guidance. Decisions will drive the prioritization of activities of T13.2 (VP evolutions) and T13.3 (onboarding resources) to allow WPs 14, 15 and 16 deliver services by which RD researchers can contribute to the ERDERA Data Hub as a value proposition. Care will be taken to ensure that strategic steering remains high-level so that the operational teams can achieve optimal usable results.

The strategic prioritization of the DSH activities will be done in cooperation with the global ERDERA strategy (T1.2) to ensure that services developed between projects and the DSH remain aligned with the SRIA specific objectives, and with the ERDERA overarching prioritization. Strategic interactions will occur during the AWPs preparation and at any time unplanned needs arrive and require prioritization decisions that may have an impact on the ongoing service delivery. It will contribute to the mentoring and consultancy services (WP17) to ensure that all ERDERA expertise is applied in

optimizing contributions to the ERDERA outputs. Special attention will be given to the cooperation with other European and international initiatives such as EHDS, EOSC, EU Platform for RD registration, ELIXIR, 1+MG/GDI, C-Path, GA4GH, etc., as they are required to operate projects during Year 1. In addition, this task will ensure cross-talks with the ERDERA ELSI, IP, regulatory services, as well as sustainability strategy (T1.5) in relation to aspects relevant for the VP ecosystem, such as data controllership, data access, data sharing, data privacy, intellectual property, and licensing.

Operationally, T13.1 will process incoming needs or requests (demands), should they come from Funding research and CRN workstreams, from external users, or internally from other Data Services Hub teams. The first incoming needs will be collected as a backlog by the Project manager in coordination meetings with DSH WP leaders, WS leaders (CRNs, Funding research, National and international alignment, Acceleration Hub). Contributions to the VP evolution (services or new resources) will be organized in regular sprint meetings at most one month apart. Development cycle (Sprint) meetings will be organized virtually monthly to decide on the work to be achieved by T13.2 (VP evolutions) and T14.3 (onboarding resources), and WPs 14 to 16, as well as to monitor the performance of the former sprint. Technical decisions in the agile process will be overseen by the acting CTO (WP co-lead Luiz Bonino). Decisions with potential impact on strategic DSH goals will be evaluated by T13.1 leaders and the CTO, including an assessment of the feasibility (effort needed and impact) and the criticality for the data objectives of the ERDERA. Demands and developments will be traced in GitHub or a similar tracking system. The task monitors that the needs and requests feed into an agile, user-centric cycle of defining user stories, designating product owners, and delivering services and onboarded resources in test-develop-feedback cycles. A common factor in line with the DSH strategy is that services must support increasing growth of the VP. ser
Service provision to **Year 1** case studies (demands) according to this methodology will allow to set the baseline for further scalability over the forthcoming years, towards progressive delivery of services for most or all the CRN activities & ERDERA funded research by the end of this partnership in a consistent, standardized way. **At the end of Year 1,** the strategic and operational decision-making processes will be set up, to ensure that the DSH as a whole runs in an aligned and efficient way.

T13.2. RD-VP evolution and scaling up (M1-M12) *TL: UTWENTE, AIT; Contributors: INSERM_Orphanet, BBMRI-ERIC, UPM, GUF, UMCG, LUMC, ULEIC, CNAG, UKLFR, QUB-UK**.
T13.2. aligns with GO:1-3; SO:1-5; OO:2.
This task has two main responsibilities:

- Maintain and evolve the RD-VP's architecture and specifications.
- Overlook the developments to guarantee that they conform with the VP's architecture.

The steering and prioritization of connecting new resources to the RD-VP and new functionality for the platform defined in T13.1 will require adjustments to the RD-VP's architecture design and, consequently, to the platform's specifications. T13.2 then analyses these new requirements for the platform based on the characteristics of the new resources to be connected, design the new functionality, and updates the RD-VP's architecture and update the RD-VP's specifications accordingly.

Once the updated architecture and specifications are released, T13.2 overlooks the implementation of the changes on the impacted components, software applications and services to guarantee conformance with the specifications. Moreover, T13.2 collaborates with T13.3 to guarantee that the onboarding of the new resources occurs based on the latest design and specifications.
In summary, the activities of this task include the following:

- Curation and evolution of the Virtual Platform's architecture and specifications [UTwente, AIT] in collaboration with all involved partners and T13.1, T13.3.
- Overarching technical development management of the Virtual Platform [UTwente, AIT] to guarantee compliance of the developments with the VP's architecture and specifications in collaboration with the stakeholders responsible for the developments.

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- Service-oriented evolution of components, including VP Index evolutive maintenance [UTwente, LUMC], metadata and data models updates [UPM, UTwente, LUMC, QUB-UK], AAI and consent [UMCG, BBMRI-ERIC], PPRL interoperability [AIT], core INSERM_Orphanet services [INSERM_Orphanet], discovery services based on Beacon framework [UMCG, ULEIC] and distributed analysis services [UMCG, UPM, LUMC].
- VP Portal: Maintenance (e.g., bug fixes, security, and software updates) and upgrade of the VP Portal functionalities [GUF], integrate WP16 knowledge bases and collaborate with the ERDERA website service provider for the user interface.

At the end of Year 1,

- A revised version of the VP architecture specifications (including expanded metadata and data models, standards and requirements) will be delivered as a baseline for the subsequent work in the ERDERA.
- A fully operational VP allowing for deep federated query and analysis based on selected use cases supporting some of the CRN case studies (based on the 13.1 prioritization) will be delivered.

T13.3. VP onboarding services (M1-M12) *TL: UMCG, UPM; Participants: SRUMC, LUMC, AUMC.* T13.3. aligns with GO:1-3; SO:1-5; OO:2.
This task is responsible for the maintenance and evolution of the documentation, services and support to onboard resources into the RD-VP. Based on the steering and prioritization of new resources to be connected to the RD-VP conducted by T13.1 and the specifications of the RD-VP defined by T13.2, T13.3 engages with these resources to offer support for the onboarding process. **In Year 1,** it is expected that the first outputs of WP16, namely the PCOMs repository, the Treatabolome and knowledge bases and ontologies as they are released, will be onboarded in Year 1, as well as the ERDERA data platform (ST1.1.4) and the knowledge Hub (monitoring system platform, ST1.3.1). Data sources and analysis platforms entering in collaboration with WP14 and WP15 will also be progressively onboarded from Year 1**.** Completion of Solve-RD data infrastructure onboarding will be achieved.

According to the case studies, automated onboarding services will be developed: To assist new resources who request onboarding, this task will start the following developments during **Year 1** and test them on a subset of low-hanging fruit resources, selected on their readiness for one or several of the following approaches:

- Design and implement fully automated importing tools capable of recognizing a myriad of existing metadata schemas in use globally (including, but not limited to, schema.org, HCLS Dataset Descriptors, and VoID) and automatically registering them with the VP.
- Implement easy to install and operate data capture tools to connect local and networked partners desiring integration with the RD-VP, such as but not limited to MOLGENIS and similar tools for data management, and federated analysis protocols such as DataSHIELD, using aforementioned semantic templates to enable FAIR data capture at source. Enhance this "rapid bootstrapping" of onboarding requests by automated text-mining of existing Web pages to generate the semantic annotations utilized by the VP to aid discovery. DataSHIELD, using aforementioned semantic templates to enable FAIR data capture at source.

Onboarding of new resources will track closely with the requirements of WP14 and WP15 to aid in the rapid establishment of analytical pipelines through improved resource discovery.

Automation of the onboarding process and expansion into new resource types requires extra attention be given to the appropriate capture of legal and IP expectations and constraints. The Expertise Services Hub (especially WP18 Regulatory support service) will be consulted to ensure proper usage, and credit, of the onboarded resources.

The onboarding task will closely interact with the mentoring and consultancy service that integrates all ERDERA components and is designed to scale with the number of projects funded through JTC and CRN projects. In a direct feedback loop the consultancy will apply onboarding services for new resource types and provide feedback for their evolution. Conversely, the added value of onboarding will be directly demonstrable by analyses that run on onboarded resources.

Requirements for the modifications of the RD-VP, that may emerge when onboarding resources, will be discussed with T13.2 to generate the related update of the RD-VP's architecture and specifications.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**14**		**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Data readiness services**						
Short name of participant & (No)	UPM (18)	LUMC (16)	C-PATH (14)	AUMC (20)	SRUMC (11)	DDF (51)	UMCG (19)
Person Months	9	8	9	5	5	4	3
Short name of participant & (No)	UTWENTE (17)	AIT (36)	CNAG (10)	CRG-CERCA (145)	ISS (75)		
Person Months	3	3	1.5	1	0.6		
Start month	M1		**End month**		M12		

State of the art behind this WP

Being able to efficiently use and reuse data and knowledge across multiple sources, often expressed as a need for data sharing and open science, has been a long-term priority for the RD community[10,11].

The community has embraced many initiatives towards this priority. The Joint Research Centre developed a community service, the EU platform for RD registration, to register RD registries and the types of data elements that they collect. It also offers services such as SPIDER for privacy-preserving data linkage. A recent example in diagnostics is the Solve-RD project that developed streamlined processes to diagnose RDs by identifying genetic diagnostic markers in sequenced genomes (see WP6). The community furthermore embraced the FAIR principles in order to achieve higher degrees of findability, accessibility, interoperability and reuse of their data and services. Experiences from RDs' 'Bring Your Own Data' workshops have contributed to conceptualization of the 15 'FAIR guiding principles for scientific data management' in the 2016 milestone publication[12,] and to first tools for publishing FAIR metadata that can meet RD community needs[13]. The FAIR principles have seen remarkable worldwide endorsement, including from IRDiRC. The RD community, not least people living with a rare condition[14], wishes to benefit from their widespread implementation. Therefore, the EJP RD has developed specifications, data models, tools, and implementation guidance for resources to contribute FAIR data to a Virtual Platform of FAIR resources (VP; see WP13). Contributing FAIR data to this network implies that records in the data sets and the relationships between them are machine actionable for automated analysis across multiple resources. Records are automatically findable by globally unique identifiers and rich metadata, accessible by providing access protocols, interoperable with other FAIR data by providing computer understandable ontological descriptions of the data records, and reusable by providing access conditions and information about the origin of the data records. Ontologies are used for the implementation, because they provide computers with a hierarchy

of computer-understandable identifiers describing types and relations in a set of records, as well as human readable labels for these identifiers. An ontological model can span multiple types of data, such as 'F508del' (variant), 'wheelchair bound' (quality of life measure), 'only share with my MD' (access condition). Most biomedical ontologies use world wide web technology as backbone ensuring that data across multiple databases across the world become virtually linked, even if they are stored in different systems in different data formats. This accommodates the biomedical domain where it is unlikely that one standard will prevail for all types of data. The EJP RD further created mappings and conversions between commonly used data standards and ontologies (e.g. mappings for CDISC, Obo Foundry ontologies, OMOP, FHIR, etc.). A factor to scale up FAIRification of data records is to supply automated mapping services for local systems.

WP14 depends on WP13 for functional FAIR data. WP14 focuses on data records that are typically in some form of container, possibly behind a firewall. Henceforth, FAIR data records (WP14) require their container to also be FAIR in the VP (WP13).

In parallel to the efforts to making data FAIR by project, it is important to note that there are already public resources for certain types of data that make this process easy for the user providing them also with the facilities to store and share their data easily, and even analyse it. The two main resources providing the data management, sustainability, and data sharing services for genome-phenome data, but also other personally identifiable experimental data types, will be the European Genome-Phenome Archive (EGA) and the RD-Connect Genome-Phenome Analysis Platform (GPAP), both part of the EJP RD VP and resource map and key resources for the Solve-RD infrastructure. The RD-Connect GPAP is an IRDiRC recognised resource which was further developed during EJP RD (e.g., phenotyping module, completely redesigned UX/UI, many new functionalities, automations, adaptation to GRCh38, connection to other resources and the VP, etc.). It will be key to harmonise the data collated by the CRN and funded projects. The EGA is an ELIXIR recommended resource which in Solve-RD has played a central role for the management, distribution and controlled access of the data, centrally and beyond the project. In the B1MG project, federated instances from both the EGA (Federated EGA; FEGA) and the GPAP were used, among other services, for the Proof of Concept to show how federated data discovery and access of RD data for 1+MG could work.

A major next challenge for the RD community is to enable scaling up the application of services to make more data ready more efficiently for more types of analyses.

Methodology

Data readiness services will be provided through an interdisciplinary, collaborative methodology, guided by strategic guidance from WP13. WP14 contributes to the co-creation of services (protocols, guidelines, project organisation) for preparing data (T14.1) and to the development of data readiness tools (T14.2). For this purpose, a team is formed by a CRN or a funded project, and WP14. In particular, WP14 contributes to the efforts of the project to also prepare and augment data for reuse by others in ERDERA, enabling simple queries to advanced automated analysis across multiple types of data stored in multiple locations. The scope is data records. The FAIRness of their container (local database or repository) and the specifications for communicating between containers in a network are the scope of WP13. WP15 will provide requirements of analysis platforms and algorithms, and WP16 will provide guidance regarding interoperability of ERDERA outcomes with the knowledge bases of WP16. The contribution from WP14 constitutes a further 'ERDERA top-up' for the project teams to contribute to the ERDERA-DH.

The data readiness services and tools that ERDERA projects produce in collaboration with WP14, facilitate resources to contribute FAIR data to the ERDERA-DH. They enable resources to give access to their data, their data exchange formats, their APIs, and their data record access conditions (if any at that level) in terms of ontology-based machine actionable models. At the highest level, automation 'agents' can interpret this information and perform appropriate actions accordingly.

This WP will also provide data ingestion services through resources further developed and adapted to RDs in projects such as EJP RD and Solve-RD. FAIRification methods that are to be applied 'at source' will be incorporated in existing procedures and tools as much as possible.

Objectives

The overall objective of this WP is to expand the use of services by which RD partners contribute to the ERDERA's robust infrastructure of data, resources, and expertise (SRIA OO2) to accelerate the automated ethical and legal exploitation of the healthcare and research data from their projects (based on guidance from WP1 and WP17-19), boosting scientific and regulatory evaluation and healthcare delivery (SRIA SO2).

Specific objectives for Year 1 in this WP are:

- To provide the requirements and design the workflow, including a first evaluation for RD partners to efficiently organise interdisciplinary data readiness teams executing FAIR data creation and FAIR data processing customised to their project to accelerate the expansion of the robust ERDERA data and knowledge infrastructure, 'the data hub', supporting in-project analysis, federated learning and AI across projects, and the regulatory pathway in drug development, paving the way to fully develop this objective in next years;
- To provide a first prototype of design of project ingestion tooling starting from the design of different tools coming from previous projects and developments, selecting the most appropriate, so in the next years tools, semantic data models, and specifications that enable RD partners to automate making data records that they manage ready to be findable, accessible, interoperable, and reusable for their project and for accelerating reuse by others via the ERDERA Data Hub, and where needed: initiate and monitor the development of missing tools, models and specifications;
- To study the data kinds and quality (RWD, synthetic, clinical trial collected) Needed in at least 2 pilot cases coming from WP9, and improving the interoperability of platforms for this purpose in other work packages to prepare for first application to the pilot cases after Year 1, providing tools and services for RD partners to prepare data for the regulatory pathway in drug development, in collaboration with WP18, including clinical collected data and synthetic data;
- To start the contribution to the design and use of a data hub personal data control that guarantees that individuals can have access to data records derived from them and, to set data record use conditions.

Description of Programmed Activities

T14.1. Services for making data findable, accessible, interoperable, reusable for automated applications (M1-M12) *TL: SRUMC, AUMC; Contributors: LUMC, UTWENTE, UPM, WDO, ISS, CNAG, FGB.* T14.1. aligns with GO:1-3; SO:2,4,5; OO:1-5.

This task focuses on providing a workflow by which RD partners increase the exploitability of the data that they manage for their project and for the ERDERA, building on previous work. The task starts with defining an initial landscape of FAIRification needs across the ERDERA projects, in order to smartly plan a FAIRification strategy that incorporates the demand of the ERDERA well as the requirement to increase capacity by delivering scaling-up methods.

Following the landscape analysis, a staging plan will be made. As the project progresses, the required WP14 capacity required to contribute to projects making data ready should decrease. Thus, as the project progresses, we should see an increasing number of data type categories that are being FAIRified, while for WP14 R&D an increasing number of different data types will be handled for one running use case. **The Year 1 will be focused on:**

- Requirements and FAIR implementation choices for data are identified. Therefore, online 'Data for Machine' workshops are organised, and workshops to define the boundaries of responsible research. The aim of these workshops is to identify existing practices and define new agreements on how to implement FAIR principles for the data records in a project or

community. From there, a data readiness plan is defined, and a team is formed between the ERDERA projects and WP14 specialists.

- Following the data readiness analysis, a project-specific data preparation team is organised together with the ERDERA project, WP13 and incorporating advice from the mentoring and consultancy service (WP17). They run in agile cycles. WP14 adds data readiness experts, and additional experts as needed.
- Data readiness workflow will be evaluated and refined, both on the direct outcomes of the workflows in terms of better prepared data, as well as to what extend the workflow leads to accelerated adoption and prepare for Year 2 and 3 the implementation and support for real time and advanced data analysis on better prepared data.

T14.2. Data ingestion tools (M1-M12) *TL: UMCG, UPM; Contributors: AUMC, LUMC, SRUMC, AIT, CNAG, CRG-CERCA.* T14.2. aligns with GO:3; SO:1-3,5; OO:1-3,5.
This task focuses on providing broadly applicable tools that are used by the data readiness teams to accelerate the usability of data in the VP network of resources. Data are made usable for responsible federated analysis on connected computing and analysis facilities. It builds on services and standards previously developed.
The Year 1 will be focused on:

- Providing the design of project ingestion tooling starting from the design of different tools coming from previous projects and developments, selecting the most appropriate.
- Implementing a first prototype with the needed improvements to allow clinical cases to ingest data to run their experiments, at least for clinical data (tabular). This first version will be improved and completed with more data categories ingestion tools and evolution of the selected tools.

T14.3. Services for advancing the regulatory pathway in drug development (M1-M12) *TL: C-PATH, DDF; Contributors: WDO, LUMC.* T14.3. aligns with GO:2; SO:2,4,5; OO:1-5.
The development of existing and new predictive tools and methods that would qualify as Drug Development Tools (DDTs) require regulatory and data science strategies at design and planning stage to accelerate implementation of novel technologies, innovative trial design and the use of Real-World Evidence (RWE) in study design and medicines developments, besides the acceptability and validity of synthetic data, especially in ultra-rare diseases.
This task aims to maximise the use of data to develop tools, accessible to the community, for optimising and accelerating drug development for RDs. Such data should be in a regulatory-grade format and FAIR (T14.2), suitable for analytics, ensuring the quality of data, and enabling re-use of data. **The Year 1 will be focused on:**

- Studying the data kinds and quality (RWD, Synthetic, clinical trial data) needed in at least 2 pilot cases coming from WP9 and improving the interoperability of platforms for this purpose in other WPs.
- Study the re-usability and shareability of data.
- Prepare for first application to the pilot cases.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**15**	**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Data sharing and analysis services**					
Short name of participant & (No)	UMCG (19)	CAD (1.1)	CNAG (10)	UPM (18)	UU (121)	ULEIC* (171)	IMAGINE (70)
Person Months	26	14.5	13.5	8.25	7.25	5.5	4.5

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Short name of participant & (No)	CHEO-RI* (151)		
Person Months			
Start month	M1	**End month**	M12

**Associated partners providing in-kind contribution*

State of the art behind this WP

WP15 starting point is the reuse of existing resources, tools, technology and methods, which will be further developed, adapted, scaled up and connected to service the CRN and funded project high data analysis needs. Key resources to reuse include high performance compute 'cloud' solutions from EJP RD, Solve-RD 'sandbox', CINECA, EOSClife; federated analysis server installations by Genomed4All, EUCAN-connect/DataSHIELD; and user facing analysis services such as the RD-Connect GPAP and MOLGENIS. The EGA will provide data ingestion and data management services through WP6 and WP14. The provision of centralized, distributed or federated analysis functionalities in WP15 will mainly rely on trusted research environments (TRE) (in Solve-RD known as the 'Sandbox', operated by UMCG with a mirror site at EBI) that may be deployed ad-hoc, portable pipelines, the RD-Connect GPAP and local implementations of the GPAP or similar platforms, as identified in WP7. The TRE is a general-purpose high-performance computing environment for bioinformatics analysis (based on Linux clusters with task scheduling) matching the common practices used by most partners, that can be cloned and scaled to match the needs of the specific group. It includes also MOLGENIS RD3, which is a track and trace database system for patients, samples, and data files used in the analysis (MOLGENIS is also used for 5 ERN patient registries). The RD-Connect GPAP enables collaborative genome-phenome analysis for research on diagnosis and novel gene discovery, including patient matchmaking. Local implementations of the GPAP may be a route for genome-phenome data federation, as used in the B1MG Proof of Concept on Rare Diseases[15]. While initiatives like 1+MG have a use case on RDs, its implementation project (GDI) does not include a RD use case and focuses mainly on the implementation of the provision of access across borders of genomic and phenotypic data[16], rather than on the analysis of the data. UU, UMCG and CRG are co-leaders of three of the GDI Vanguard (early adopter) nodes: Spain, Netherlands, and Sweden. However, efforts are being done in parallel on federated data discovery, access and analysis in international projects and initiatives such as ELIXIR, DataSHIELD, EOSC, Genomed4All, GA4GH or MatchMaker Exchange. Many of the partners in WP15 are key players in those activities, and it is expected that newer protocols, standards, tools, and APIs will become available during the ERDERA project, enabling their customization and implementation for the full range of ERDERA CRN needs, from distributed and federated large scale genomics analysis to federated analysis of clinical outcomes across the HCP.

Methodology

An advantage of the RD community is that it has broadly adopted ontologies and standards such as HPO, ORDO and OMIM, at least for clinical research, facilitating the interoperability of datasets since they are already harmonized to a certain extent. WP15 will rely on WP13 for the connection and interoperability of resources, WP14 for data ingestion and harmonization and WP16 for additional knowledge resources useful for data analysis (I.e. annotation, filtering and interpretation). The analysis needs from the CRN streams in first place, and the ERDERA funded projects in second place, will drive the developments for WP15. Sustained efforts will be carried out to cover the CRN and funded projects needs w, therefore WP15 co-leads will coordinate a working group including at least WP15 TLs and the CRN stream leaders who will meet at least every six months to discuss the analysis infrastructure requirements, and prioritise the developments and support needed from WP15, as well as acquire additional compute/storage capacity if necessary (e.g. in-kind from ERDERA partners and by forging partnerships with large public or private compute infrastructures). For example, ERDERA will strive to use EU capacities (also for GDPR compliance and data security issues) such as those from the Euro-HPC Joint Undertaking, another Partnership under Horizon Europe. Access to high

computing is not guaranteed and has to follow a standardised application process including peer review, but it is worth investigating and applying, given the strategic relevance for the sake of RD patients but also to improve EU cooperation and capacities on health data in general."

T15.1 will sustain, exploit, and adapt environments and resources created for large scale collaborative data analysis. The main three assets will be (a) a network of Trusted Research Environments (TRE) for high performance data analysis by individuals and analysis groups, (b) therein a collection of deployed analysis tools and best practice pipelines linking these tools into effective data analysis workflows to be used at scale addressing needs of the CRN and research project and (c) expansions of the a + b to enable federated multi-centre analysis as secure processing environment (SPE) where the analysis can be orchestrated across multiple data analysis sites, optionally in a privacy preserving way (I.e. without sharing patient identity data) to address ELSI and GDPR requirements. **In Years 1-3,** the priority will be on streamlining analysis activities from the CRN, scaling up from best practices developed in the Solve-RD project with contributions from EJP RD and CINECA, and the integration of best practices and analysis services from partners that were not in EJP RD. Next to providing coordination and connections to local compute facility providers in the CRN for distributed analyses (where analysis is done on in-house computer clusters by local staff), the main effort will be to operate a scalable TRE environment (in Solve-RD known as the 'Sandbox', operated by UMCG) with sufficient capacity and relevant tools for researchers from multiple centres to receive accounts and collaboratively analyse CRN data. The goal is to enable CRN to receive access to a TRE so data analysis task forces and data interpretation task forces (DATF/DITF) can effectively collaborate around the data. Main effort will be to make these environments operational with the option for projects to scale up the environment (e.g. into Azure). In addition, updates will be provided to keep the TRE up to date considering TRE developments in EOSC, EHDS and potentially GDI, and aiming for ISO 27001 certification. It will also be necessary to develop a seamless tracking system for data. Metadata, analyses, and results, tightly linked to the EGA and the RD-Connect GPAP, geared towards a clinical researcher profile. This system will be based on the Solve-RD RD3 system, mainly developed upon MOLGENIS software, and incorporating recommendations and components from FAIR genomes project (a good practice now incorporated into GDI) and Café Variome. It should be user friendly for clinical researchers and be able to integrate seamlessly with other resources (including the VP), through APIs (RDF, REST and GraphQL), a common authentication and authorization standards (LS AAI), and domain specific standards for data and discovery such as Beacon v2 and other GA4GH standards. The tracking system should enable tracking where all the generated results in the CRN are and enable to capture the feedback from the variant interpretation conducted in WP7 through the RD-Connect GPAP or other local platforms used in a federated setting. This system should be portable, with the aim that it can be installed on nodes participating in the federated analysis approaches of the CRN.

The bulk of T15.2 efforts will be directed to the implementation of portable pipelines based on CRN and JTC project prioritization. The focus will be on professional implementation and documentation of proven methods into robust and portable pipelines, such that they can be easily deployed at the connected compute centres to provide the capacity for the ambitious CRN goals (e.g. 100k genomes analysed in a distributed and/or federated manner). As many ERDERA partners already have mature pipelines, **the task will focus in Years 1-3 on integrating the best components of these pipelines and/or provide cross validation of these pipelines to ensure their outcomes can be jointly analysed,** i.e., transforming from currently parallel development efforts at national/local level (e.g. local GPAP/CNAG, MOLGENIS/UMCG VIP, PFMG, Clinical Genomics Sweden) into a collaborative network of pipeline developers reducing duplicate efforts by sharing building blocks (e.g. containers) and sub-workflows. Next to pipelines, further development and integration of annotation, knowledge, and analysis servers such as C-PATH, RD-Connect GPAP, and many more, are expected, in particular for outcome and therapeutics workstream into VP services. Especially for the GPAP, it will be necessary to explore ways of structuring the data and backend modifications that will allow the system to still ingest and query in reasonable time the amount of data envisioned in the CRN analysis and to develop mechanisms to enable federation of data and analysis. It will also be necessary to further

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develop and speed up the pyGPAP module, key for automating variant filtering and prioritization across thousands of samples and generating the integrated and user-friendly results for the DITFs.

T15.3 aims to contribute to the development and utilization of the necessary infrastructure to provide federated analysis services. ST15.3.1 will develop the necessary infrastructure and service to move from 'centralized' to 'federated' analysis of virtual patient cohorts across multiple centres. The focus will be on enabling federated execution of the analysis where patient data doesn't need to be all centrally shared but instead is processed 'at source' and only non-identifiable results are shared. This federation of 'Secure Processing Environments' (SPE) is motivated in part by ELSI and GDPR considerations, where legal and ethical considerations prohibit the data transfer of privacy sensitive data. However, via this federation it will be possible to scale up to a much larger patient sample sizes while making use of local compute capacity that is impossible to fund centrally. It will also be possible to scale up the number of repositories and registries, without the need to move data to a central server. A close collaboration with emerging EHDS developments is expected. The activities will make use of and combine emerging classes of federated analysis, such as based on semantic web technology, container based technology (e.g. where analysis pipelines as a whole are defined beforehand and when approved can be executed in the federation), distributed AI models with containers (similar, but with different ways of averaging and consolidating results based on nodes quality) and secure command based (e.g. DataSHIELD, where each command is shielded giving researcher flexibility to create new workflows without approval process) besides the federated data platform able to deploy distributed algorithms, train, execute and complete the life cycle of the AI models with the data in distributed locations. Finally, via this federated approach the ST to create user friendly 'bundles' of data analysis tools that can easily be deployed on premise or make use of HCPs for initial model training and parameter consolidation. DataSHIELD
In Years 1-3, ST15.3.2 will map the CRN needs on federated analysis with the technical solutions already proposed and/or available in international projects and initiatives such as 1+MG/GDI, ELIXIR, EOSC, Genomed4All, GA4GH, MatchMaker Exchange etc. It is likely that it will not be possible to even visit the data from the participating partners that cannot contribute data for the distributed analysis. This will call for federated approaches in which coordinated queries or analyses will need to run where the data is being hosted. The needs-to-solutions mapping will lead to the definition of two use cases and the preparation of a technical plan for federated analysis together with WPs 6-8 and ST. This will be followed, still **in Years 1-3**, by the initial technical developments to make this possible and showcase the use cases. It is envisioned that the developments will need to focus on one-sided and zero-sided matchmaking as well as enabling machine learning models to be trained in a federated manner, collecting the non-identifiable results centrally. Collaboration with the CRN will also be a key point to understand how coordinated interpretation of variants can be made while still preserving the privacy of the data. In Years 4-7, the aim will be to collaborate on 2 proof of concept use cases on federated learning. Although further discussion will be needed, the first one could aim to discover new potential gene-disease association thanks to the increased sample size of all the independent datasets. The second one may aim to look for modifiers in those cases that have already been molecularly diagnosed, considering the different clinical presentations that mutations on the same gene can present.

Objectives

The overall objective of WP15 is to provide an up scalable and distributable data analysis infrastructure to serve the CRN and funded projects prioritised needs.
The specific objectives of WP15 for AWP1:

- First release of analysis ready reference deployments of the ERDERA analysis infrastructure, including support and interoperability with WP13-15 data ingestion, and ability to scale to cloud computing matching CRN prioritised needs;
- Collect and develop protocols, software and pipelines for large data sets and high-performance computing (HPC) analyses and deploy to the infrastructure, with priority on CRN first analysis objectives;

- Collect and develop protocols, software and systems that enable federated data analysis use cases and pilots, with focus on a demonstrator that integrates the main federated analysis frameworks.

Description of Programmed Activities

T15.1. Data analysis platform deployment (M1-M12) *TL: UMCG, ULEIC*; Contributor: CNAG, AIT.* T15.1. aligns with GO:1-3; SO:1,2,4,5; OO:1-5.
This task will provide the coordination and integration of WP15 services into a ready to use operational infrastructure for ERDERA data analysis (see tasks below) through key resources, i.e., high performance compute 'cloud' solutions from EJP-RD, Solve-RD 'sandbox', CINECA, EOSClife; federated analysis server installations by Genomed4All, EUCAN-connect; and user facing analysis services such as the RD-Connect GPAP (or local GPAP installations) and MOLGENIS. The infrastructure consists of portable and interoperable packages, including SOPs, such that they can be installed and scaled up by ERDERA partners on-site or on external (cloud) providers (at a fee for service). A key development of the task will be a system to track data, metadata, analyses, and the genomic variants interpretation workflow, mainly for the CRN Research Diagnostics stream, according to the technical requirements exposed in WP13. This tracker will be based on RD3, initially developed in Solve-RD, and should be user friendly for clinical researchers and be able to integrate seamlessly with other resources (including the VP), through APIs (DCAT/RDF, Beacon, Café Variome) and a common AAI, making it suitable for both a distributed and a federated approach. This will be supported by the knowledge base, ontologies and data models coming from WP16 which will support the analysis by providing the required based against to validate the results, and to feed the AI models. In addition, this task will also provide a reference deployment of the ERDERA analysis infrastructure, including helpdesk and support to onboard users from the CRN and funded projects. The task will also contribute to data interoperability to other WPs in the Data Services Hub, in particular WP14 for data sharing and ingestion. These reference deployments will have limited computing and storage resources provided in-kind by the task contributors. However, they will be designed to be easily scaled up using cloud technology based on CRN and funded project needs and own available resources. The central reference deployments and partner installations will then have the possibility to be connected into a federated analysis network.

In Year 1, developments covering the different data categories defined in the project and processed in WP14 will be made available. First operational templates for the high-performance compute nodes and federated analysis nodes will be released, revised, and integrated from previous projects, and deployed on two clouds, ready for developers and users of T15.2 and T15.3. In addition, data service interfaces, operations and support tools and processes will be implemented. In particular for genomics the RD-Connect GPAP will be available from the beginning to conduct genome-phenome data analysis of data ingested in WP14. For other "omics" such as radiomics, proteomics, etc. and for clinical information GenoMED4ALL distributed data platform will be available. Both approaches will converge in the first months. **Further developments will be necessary in Year 1,** starting with the improvement of the pyGPAP module to automate analyses for the CRN and keep track of the conducted analyses, which will facilitate the provision of a reduced number of variants for interpretation to the Data Interpretation Task Forces as well as the modules, besides other improvements to other omics and clinical info to satisfy WP13 collected requirements. For the development of the data and analysis tracking system the needs and specifications from the CRN streams will be collected. As example for genomics the system will be based on the MOLGENIS/RD3 system developed in Solve-RD, with Café Variome discovery interface, to be expanded for cover prioritised CRN needs with WP13-14, and a reference deployment will be functional from the beginning albeit if not with all the functionalities, which will be developed to make it more comprehensive, automatic and user-friendly. For example, it will be necessary to automate the metadata uploads from the RD-Connect GPAP and the EGA. The development will be done in sprints, with the involvement of the user in every step of the process.

T15.2. High performance compute pipeline and 'cloud' services (M1-M12) *TL: UMCG,CAD; Contributor: CNAG.* T15.2. aligns with GO:1-3; SO:1,2,4,5; OO:1-5.

This task will provide services for large scale analysis, setting the standards and integrating and maintaining best practice analysis pipelines that require 'high performance computing' (HPC) such as genomics, AI and radiomics, building on key resources from RD-Connect GPAP/CNAG, MOLGENIS/UMCG VIP, PFMG2025, Clinical Genomics Sweden, and analysis services such as C-PATH and Orphascape-phenotypic similarity variant prioritisation besides incorporating results from funded projects such as GenoMed4ALL (see T15.3), and aligned with EOSC, EHDS and ESFRI developments. The bulk of the work will be focused on integrating methods prioritized by CRN and funded projects into portable and interoperable HPC analysis pipelines so these methods can be applied at scale. Initially the focus will be on genome diagnostics research pipelines, but it is expected that also computationally intensive pipelines will be needed for outcome and therapeutics research, such as to include new AI approaches, semantic web data analysis to enable federated learning and/or radiomics (see also T15.3). In addition, the task will deliver a 'HPC' in a box template ('starter kit') that will be deployed into T15.1 as a basis for reuse of ERDERA provided services either as a service or as open-source best practice. Finally, this task will provide the tools to link and operate a network of analysis nodes to enable first distributed and later federated analysis between the ERDERA partners. The start will be with key CRN genome diagnostics research centres as described in WP7 and then scale up to support the federated network use cases from T15.3. The addition of new analysis nodes will be supported (e.g. to serve JTC projects, using either institutes facilities or public/private cloud servers). The expectation is to complement and make use of developments from already funded projects such as GDI project (e.g. authorization via LS AAI), which provides Genomics data access infrastructure components but offer no analysis capability.
In Year 1, the partners will collect the high-performance analysis needs from the CRN streams, and in particular from T7.1 for the coordinated genomics analysis pipeline and deliver first pipeline releases in time to process the first batches of CRN datasets. These needs will be prioritised together with the CRN partners using agile/scrum methods, considering as one of the factors the availability of some pipelines and the effort to develop new pipelines based on recently established best practices. The expectation is to initially serve genomics diagnostics analysis requirements, but also to address some large analysis needs for clinical and therapeutics research, such as machine learning. It is expected that in some cases it will not be necessary to develop new pipelines but rather package existing pipelines in a way that they can easily be installed locally for distributed and/or federated operations or be scaled to cloud. When appropriate, the tools will be containerised using industry standards (e.g. Docker or Singularity) and the pipelines will be coded using widely accepted workflow languages such as Nextflow or CWL. Appropriate metadata standards will be used to record pipeline executions, to interface with RD3 and ERDERA overarching data infrastructure, including publication to ELIXIR tools catalogues to increase impact. In addition, the task will catalogue the storage and high-computing capacity provided by partners to be used for CRN objectives, such as those in the CRN Research Diagnostics Stream and the partners, aiming to contribute to the federated analysis approaches, such as FPMG and UU.

T15.3. Federated analysis (M1-M12) *TL: UPM, UU, CNAG; Contributor: UMCG,CAD, AIT, IMAGINE, CHEO-RI*.* T15.3. aligns with GO:1-3; SO:1,2,4,5; OO:1-5.
This task aims to upscale the analysis infrastructure in a federated fashion, starting from a distributed deployment of T15.1 and T15.2 assets and then implementing the methods and infrastructure components for federated analysis of clinical datasets (ST 15.3.1) and genome-phenome data (ST) to realize intra-European and cross-continental analysis capability, starting with large datasets relevant to CRN and JTC projects, aiming to a sustainable approach. **In Year 1,** T15.3 will, in collaboration with T15.2, deliver an initial proposal for federated data processing and analysis. This proposal will include the analysis of tools leveraged from previous funded projects and the suitability analysis, with a balanced approach according to the WP13 requirements elicitation.

ST15.3.1. Federated analysis and federated learning infrastructure *STL: UPM, UMCG; Contributors: IMAGINE.*
To address ELSI and GDPR issues, as well as to address scalability issues with centralized analysis, this task will implement federated analysis protocols where, instead of sharing sensitive patient data,

analyses are automatically distributed to data holders and only the training parameters and anonymous summary results are shared. The focus will be on methods and protocols which can handle and deploy the analysis in a distributed manner in an automatic parameterizable and adaptive manner according to the clinical needs.
Two directions will help this result (starting from previous existing developments in past projects and initiatives) which will be combined in the implementation: semantic federated analysis approaches from EJP-RD, DataSHIELD networks perfect for tabular outcome data as used by several ERDERA partners, which will be supported by the ontologies and knowledge bases in WP16, and Genomed4ALL methods and protocols in particular suitable for multimodal categories of data such as genomics/radiomics methods merged with clinical data, supported and/or fed by the WP16, WP14, WP9 and WP10 diseases knowledge and data models and categories, besides others which can come externally or in a later project stage. Initial focus may be on clinical outcome and therapeutics research in the CRN because these data are relatively small but very sensitive, and therefore easier to acquire local servers for within HCP (see T15.1), however expect to also scale up to AI and omics. Its implementation will be closely aligned with EOSC and EHDS projects, in particular those on SPE – Secure Processing Environment, TRE – Trusted Research Environments, GA4GH TES task execution services, LS AAI, and GDI network, considering emerging AI needs.
In the initial draft proposal to be developed in Year 1, it should at least include established federated frameworks for semantic web based federated analysis, R statistics-based analysis (e.g. DataSHIELD), and for container based analysis (e.g. Genomed4ALL). In addition, components that are to be shared between these federated analysis frameworks will be deduplicated and integrated, such as service federated authorization and authentication (e.g. using Life Sciences AAI), standardized methods for provisioning data access to federated protocols, central user interfaces for researchers (e.g. including Jupyter notebooks and RStudio), and the first release of the 'local bridgehead' package (I.e. the service that institutes can install if they want to make their data available for federated analysis). A high priority will be to minimize operational complexity and costs for hospitals/institutes deploying a federated data access node, e.g. by providing automated software updates. **At the end of Year 1,** a first integrated SW architecture and demonstrator will be ready to be tested with CRN use cases before moving to the full development. The federated analysis services will be able to cope with the data kinds defined in the project and commented in T15.1

ST15.3.2 Technical support for international federated genome-phenome analysis for research *STL: UU, CNAG Contributors: CAD, CHEO-RI**
In line with the IRDiRC objectives, this task will provide technical support to enable international federated analysis of genome-phenome data for research on RDs through several use cases and pilots. The task aims to facilitate bringing together datasets submitted to the distributed infrastructure with other datasets from EU countries, such as those from PFMG2025 and Sweden, in a federated manner. As the EU and international landscape evolves, additional EU datasets and non-EU datasets from UK, Canada and Australia may also participate in the activities. The task will leverage open standards and technical developments from GA4GH, ELIXIR, MatchMaker Exchange, and 1+MG/GDI. In this regard, the aim is to co-develop and evaluate solutions enabling one-sided and zero-sided genome-phenome patient matchmaking across the international network, supporting the CRN Research Diagnostic Stream, which will coordinate the analysis pipeline in T7.1. Initial focus will be on genome-based diagnostics research. Expansion to other data types and the potential implementation of federated learning will be evaluated with T15.3 during the first 3 years. Support on ethical and legal issues will be coordinated with ERDERA partners involved in T1.5 Ethics compliance.

In Year 1, one or two use cases for the application of federated analysis will be defined together with the CRN. The use cases will be included in the additional deliverable mentioned in T15.3 and will help drive the work and developments in the following years. **In Year 1,** the task will also focus on the scoping of available solutions and timeline from 1+MG/GDI, GA4GH, MatchMaker Exchange, ELIXIR, and other relevant projects such as Genomed4All. The different options already available or under development will be considered for the additional AWP1 deliverable indicated below.

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Additional deliverables *(additional to those included in part B of the proposal)*
Draft proposal for the application of federated data processing and analysis services in ERDERA. - M12 (UPM, CNAG, UMCG).

Set of Activities Number	**16**		**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Knowledge bases and ontologies for RD research**						
Short name of participant & (No)	INSERM-U974 (1)	INSERM_Orphanet (1)	MRT (79)	Sonio (102)	UM (21)	AMU (37)	LUMC (16)
Person Months	7.2	21.6	9	9	12	3	2
Short name of participant & (No)	CNAG (10)	AUMC (20)					
Person Months	9	10					
Start month	M1		**End month**	M12			

State of the art behind this WP

Ontologies and knowledge bases are pivotal in medical practice and research, offering structured frameworks to manage information, enhance decision-making, and improve data interoperability. Several European projects demonstrate how ontologies can address the challenges of data heterogeneity, interoperability, and knowledge representation in the healthcare domain, namely Electronic Health Records for Clinical Research (EHR4CR), SemanticHealthNet, Translational Research and Patient Safety in Europe (TRANSFoRm), Personalised Patient Information for Clinical Decision Support (p-medicine) and the European Electronic Health Record Systems (EURECA) project aiming at establishing a common framework for electronic health records across European countries and presupposing adoption of common ontologies and classifications, like Human Phenotype Ontology terms, ORPHA codes and others. Knowledgebases are organized and dynamic collections of information about a particular subject where data from multiple sources are not only archived, but also reviewed, distilled and manually annotated by experts (https://doi.org/10.12688/f1000research.12989.2). These digital infrastructures are essential to the effective functioning of scientific research and serve as a reference corpus of semantically interlinked data to be re-used in combination with research data to generate new knowledge.

By showcasing the practical benefits of knowledge bases and ontologies in clinical practice and research, they contribute to adopting standardised approaches that improve patient care, research outcomes, and healthcare system efficiency across Europe. Recently, projects like ERICA provided a curated Patient-Centred Outcomes Measures (PCOMs) repository for RD based on Orphadata Science knowledge base, EJP RD produced curated RD workflows and networks based on system biology approaches and Solve-RD provided tools for data exchange and analysis regarding phenotypical and genotypical information, complemented with a knowledge base on available precision-medicine treatments for RDs through the Treatabolome, and using standard ontologies like HPO and ORDO. This is progress towards shorter diagnosis and treatment delays for patients while increasing trial-readiness and cohort identification for emerging therapies. Healthcare and research for treatments are pivotal concerns for patients, clinicians and researchers and need to be developed into a general framework implementing universal data-sharing mechanisms.

Such mechanisms depend on harmonisation of federated patient data and knowledge resources. While many of such resources exist, their optimal use is hampered by fragmentation and lack of alignment across resources. To expedite data and knowledge sharing, this WP focuses on establishing an infrastructure through which knowledge resources can be harmonised, made available, and used e.g. in the form of queries or knowledge graphs (RD networks). This will provide an important enhancement to the virtual platform that has been developed in EJP-RD, and reusable, reference to be integrated in ERDERA-funded projects (in JTCs/CTs and CRN case studies).

Methodology

The virtual platform is meant to be the access point for knowledge bases pertaining to RDs allowing researchers and clinicians to explore diseases, molecular entities, treatment options as well as research resources (cell lines, animals, cohorts) in an integrated fashion. This WP is aimed to create new and align or improve existing knowledge bases and ontologies that have been identified as needed in previous projects, regarding Patient-Reported and Patient-Centred Outcomes, antenatal phenotypes, Treatabolome, RD maps, and ontologies, in collaboration with funded projects and CRNs. We also support their use and application by the clinical research community by providing concrete applications. The WP will closely interact with the mentoring and consultancy service that integrates all ERDERA components and is designed to scale with the number of projects funded through JTC and CRN projects. Concretely, funded research projects in WP3 and clinical trials WP4 are expected to use PCOM/PROM and antenatal phenotypes knowledge base and ontologies to annotate data and investigate and prioritise molecular targets of RD using RD networks. In an incremental approach, WSs drive Data Services Hub (DSH) activities, DSH output of increasing maturity will be made available for testing and use in the WSs, iterating towards the federated approach with fully established DSH infrastructure. This will be executed in collaboration with WP6-8 and will be sustained with concrete applications to go from one or more genetic variants to RD molecular networks, existing treatments, and better knowledge about less common genetic variants in the same pathway can help discovery of causative gene(s). WP9 and 10 drive identification of PCOM/PROM in the PCOMs repository, data annotation with PCOM/PROM, RD functional impacts and antenatal phenotypes as well as linked data/RD network applications and ontologies for concrete research questions. We support research on innovative therapies in WP11 and 12 by providing data annotation, molecular pathways, and networks to investigate molecular causes of how treatment works and compare with existing treatments (Treatabolome). **To enable co-creation and ensure the service needs are met a concrete task for Year 1, AWP is to set up communication infrastructure with other workstreams and plan a workshop around design and content of the RD map services with CRN and funded project partners (JTC and EJP RD).** In order to further fulfil the needs of CRNs and funded projects, this WP will also contribute to the education and training activities (WP20) and support the Expertise Services Hub (WP17-19) with tutorials, workshop organization for training on knowledge bases and concrete applications or hackathons to solve concrete questions.

Concretely, this WP contributes to fulfilling the following needs: 1) for the virtual platform to connect existing data, it provides a means to query data represented using the variety of terminologies and ontologies geared towards healthcare and the RD domain, by providing semantically rich mappings across those terminologies and 2) for initiatives to collect new or broader data sets (including CRNs WP9, 11 and 12 and funded projects) it provides services to establish data sets that are harmonised upfront, maximising their reusability and their linkage to other resources, and queryability in the virtual platform.

Objectives

Specific objectives for Year 1 are:

- Establish workflow and communications with other WPs/WSs for cooperation and co-creation
- Collaborate on defining first research question for RD maps towards Year 3 proof-of-concept
- Start specifying the requirements for use of the specified knowledge bases
- Assess interoperability needs of knowledge bases to be connected to RD maps

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- Start work on alignment of incorporated knowledge resources

Description of Programmed Activities

Year 1 activities will focus on getting the individual tasks started, and establishing collaboration and communication within ERDERA, both across WSs and within the Data Services Hub.

T16.1. Evolving a repository of FAIR Patient-Centred Outcome Measures (PCOMs)/ Patient-Reported Outcome Measures (PROMs) (M1-M12) *TL: INSERM_Orphanet, MRT; Contributor: AUMC.* T16.1. aligns with GO:3; SO:1-3; OO:1.
This task will leverage on one of the major outcomes of the ERICA WP3, providing a curated PCOMs repository for RD. The RD PCOMs repository is currently accessible from the ERICA webpage and its content is hosted in a larger PCOMs database (PROQOLID™) and maintained by MAPI Research Trust and Orphanet. **In Year 1**, we will onboard the current repository in the Virtual Platform (WP13) and work towards a hosting solution that is sustainable beyond the duration of the ERICA project. WP16.1 will ensure continuous implementation of new PCOMs identified in open consultation for external input, in literature reviews performed by Orphanet and MAPI Research Trust and in other WPs like PCOMs developed in the frame of T10.1. The development of 2 search functionalities will be performed:1/identification of PCOMs for diseases within a functional cluster (sharing the same functional impact profile) and 2/identification of PCOMs matching functional concepts to be assessed, i.e., in a clinical trial. For the first search functionality, in ERICA, the Orphanet knowledge base on functional consequences of RD (see T16.5) was used to create clusters of RD based on their curated functional consequences profiles to identify suitable PCOMs for validation in other diseases than those for which they were originally developed, to promote their repurposing. **In Year 1**, quality control of the RD functional clusters will be organized with ERNs and patient organisations in a systematic way. For the second search functionality, in the ERICA project, an algorithm using Natural Language Programming (NLP) has been developed to automatically allocate ICF code to items of PCOMs listed in the repository. ICF-coded PCOMs could be matched with ICF-coded RDs, annotated by Orphanet. **In Year 1**, we will extract PCOMs items and the quality of ICF coding generated by NLP will be assessed.

T16.2. Antenatal echographic and pathologic RD phenotypes knowledge base and ontology (M1-M12) *TL: INSERM_Orphanet, Sonio.* T16.2. aligns with GO:1; SO:2; OO:1.
Whereas RD postnatal phenotypes are well described and made re-usable as ontologies (ORDO, HPO and the ontological module HOOM, see T16.5), there is no reusable ontology for antenatal phenotypic abnormalities that have the potential to facilitate antenatal echographic suspicion and diagnosis of a RD to trigger decision-making, including genetic testing based on diagnostic suspicion, pregnancy continuation, in utero treatment, post-natal early care and genetic counselling. The aim of this task is to leverage on the knowledge being generated by the software and AI for prenatal diagnosis of RDs and congenital malformations developed by Sonio, based on academic foetal medicine research, to produce an ontology of phenotypic annotations corresponding to detectable RD antenatal abnormalities, by proposing extensions to the HPO (or developing a stand-alone ontology if needed). This ontology and annotations will increase the Orphanet content, making it freely available as part of Orphanet's Orphadata Science[17], which is a Global Core BioData Resource. An ontological version of these antenatal phenotypic anomalies of RD will be developed based on the current HPO-ORDO ontological module (HOOM). The curation will be done in collaboration with ERNs and foetal medicine experts contributing to this task. This reference ontology will offer a computable reference dataset to be reused to foster RD diagnosis by contributing to, amongst other, variant prioritization phenotypic-based algorithms. **In Year 1,** a controlled vocabulary for echographic signs will be established, based on the content already retrieved by Sonio, and a repository of annotations of RD

using these terms will be initiated, by organising the curation cycle with RD experts in CRNs and foetal medicine external experts. Alignment with HOOM and other knowledge resources will be investigated.

T16.3. Treatabolome (M1-M12) *TL: CNAG, INSERM_U974.* T16.3. aligns with GO:2; SO:1-3; OO:2.
The Treatabolome is an interdisciplinary collaboration between disease experts and computational experts designed to make expert information about existing RD treatments more readily accessible. The Treatabolome DB already contains 3623 entries from 745 publications and is publicly accessible through programmatic interfaces and a web portal, and its expansion through this work plan will focus on improving both its disease coverage and its interoperability and linkage with other systems. With guidance from an expert committee to ensure maintenance of the evidence base for all data entered, we will upgrade the current system, develop a systematic method and schedule for updating existing datasets to maintain currency of information, develop an online interface for crowdsourcing and expert curation of treatment-variant and treatment-gene assertions, integrate additional FAIR functionality into the Treatabolome DB including new ontologies (e.g. MAxO), include deep phenotyping and increase phenotype granularity by improved clinical data and HPO and ORDO linkage, and link known targets within the Treatabolome with molecular pathways and RD networks for mechanistic explanation of how treatment works. This task aims to further expand and develop the Treatabolome infrastructure to increase the number of RDs covered and improve the data capture and curation infrastructure to deal with larger datasets and additional methods of data capture (including crowdsourcing) while retaining its evidence-based reliability.

In Year 1, a Treatabolome steering committee (SC) will be established to provide expert clinical and technical input to guide the Treatabolome expansion. This SC will include at least 5 members with clinical and technical expertise (e.g. ontologies, genetic analysis, software development, etc), including at least 1 member from each of the task co-lead partners. The SC will work with task partners to develop an implementation plan covering updating of existing systematic literature reviews (SLRs) and commissioning of new SLRs, recommending additional data to be captured and ontologies to be used to improve FAIR functionality, evaluating existing NLP tools (in collaboration with WP14) to automate literature extraction of gene-disease associations, including variant level information as well as mapping out the technical and expertise requirements for establishment of a crowdsourcing and curation platform for data capture and review. To ensure comprehensive representation of RD expertise and optimize the approach's usefulness for end users, this implementation plan will be developed in close collaboration with ERN representatives.

T16.4. RD maps (M1-M12) *TL: UM, LUMC; Contributor: AMU.* T16.4. aligns with GO:1-2; SO:1,2; OO:2.
RD knowledge networks will start with molecular pathways capturing the molecular interactions of RD genes and their associated downstream effects leading to the distinct phenotypes. These molecular networks are now connected to the newly created knowledge bases linking molecular causes (from the WikiPathways RDF triple store and its RD community pathways) to phenotypic symptoms – PROM/PCOM and Treatabolome. Multi-dimensional networks and knowledge graphs will include potential links to chemical compounds and their interaction networks (as started in EJP RD) for identification and prioritisation of potential treatments. **In Year 1,** we will focus on different tasks to get the project started: 1. Establishing communication and information exchange with CRNs and eventually already funded projects (e.g. from previous EJP RD or JTC) to 2. Development of a first research question and draft for the first service demonstrator. 3. Assessment of the CRNs and funded projects needs in RD maps. We need to get feedback and information on what information would be most interesting to be provided in a RD map and which knowledge bases are most useful to get this information. We intend to organise a workshop together with selected partners from CRN and funded projects to answer these questions. 4. Assessment of the interoperability status of the knowledge bases prioritised for network integration and prospective for the new knowledge bases of Task 1, 2 and 3.

T16.5. Improving, creating, and expanding RD Ontologies and semantic models (M1-M12) *TL: AUMC, INSERM_Orphanet; Contributor: LUMC, UM.* T16.5. aligns with GO:1; SO:1,2,5; OO:2.
In alignment with T16.1, WP13 and the CRNs the requirements and core resources for the repository will be identified and the repository will be populated with these resources, which will be provided with explicit semantics if these are not provided natively. The repository will be light-weight graph-based infrastructure that contains ontologies as foundational layer for unique identification and specification of elements in other resources, information models and schemas based on those ontologies, and knowledge sources as selected or created in other tasks. As much as possible, the resources are interlinked so that any concepts that are specified in more than one resource, whether exactly or at different levels of granularity, are identified and properly related, preferably using the Simple Standard for Sharing Ontological Mappings (SSSOM). To maximize sustainability of the repository, including augmentation of the set of resources and keeping the repository up to date with the most recent versions of resources, light-weight procedures will be developed, in alignment with T14.2, which aims to accelerate data ingestion by using similar techniques.

In Year 1, T16.5. will make an inventory of the required knowledge resources and assess any needs for alignment and harmonization. We will establish collaborations with organizations responsible for maintenance and updating of resources, to facilitate collaborative amendments of those systems when needed. We will lay out the requirements for an infrastructure in which the knowledge resources can be linked and harmonized and represented using semantic-web representations. This includes requirements for dealing with, possibly frequent, updates of those resources. In order to extend Orphanet Rare Disease Ontology, **during Year 1** a first draft of Orphanet Functional Consequences Ontology (provisionally called OFCO) will be proposed based on the existing Orphanet Functioning Thesaurus, derived and adapted from the International Classification of Functioning, Disability and Health – Children and Youth (ICF-CY, WHO 2007) and on the Orphanet functional impacts of RD knowledge base, which will be continuously expanded in collaboration with T16.1, WP10 and RD experts and patient representatives. The collaboration with T10.1. will result in a functional evaluation core-set for selected RD. In addition, HOOM (HPO-ORDO Ontological Module) will be enriched, and the association model development improved in line with those utilized for the “OFCO” module.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**17**	**Start Date or Starting Event**	**M1: September 2024**
Set of Activities Title	**Initiation of Mentoring process and feasibility study for consultancy services**		
Short name of participant & (No)	EATRIS (22)	FGB (23)	VHIR (15)
Person Months	11	3	6
Start month	M1	**End month**	M12

State of the art behind this WP

Academic basic and translational research form the seedbed of innovation, by generating a great deal of the new discoveries in biomedical research, ranging from insights into the natural history of diseases and cogent (patient-relevant) outcome measures, to disease pathways and molecular targets of interest for therapeutic development. As such, academic researchers play a crucial role in the bi-directional flow of knowledge from bench to bedside and back, eventually culminating in the (industrial) development of novel diagnostics and therapeutics that serve high medical needs. A condition sine qua non for the smooth functioning of the eco-system is that the knowledge generated

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by academic scientists must be amenable to further uptake and development by other actors in the research and innovation value chain. By extension it is important that those academic scientists are aware of the development steps later in the value chain, and the minimum requirements for a concept, project, and dataset to continue to further development. Many areas that are not familiar territory for academics will come into play, such as manufacturing and scale-up, regulatory compliance (products), intellectual property, reimbursement. These domain expertise's are difficult to access for academics, yet interaction with them in the early phases of development are essential for later success.

With the above in mind, the mentoring program was created to provide researchers with a mix of competences in drug/diagnostic development, regulatory science, methodological, pre-clinical and clinical development, and intellectual property needed to support successful translational research, to secure follow-on funding and find partners for the development of new treatments and diagnostics for RDs. To move a research project across the pipeline that leads to market authorization and reimbursement, and remove the well-known difficulties, a multitude of different actions and different sets of competencies are necessary. This WP supports the RDs community to translate high quality research more effectively into high impact interventions for the RD patient community, by creating a bridge between basic research and medical innovation through easy access to expertise essential for successful product development.

Methodology

The translational research process works on effective development of knowledge from one system to another or from the discovery level to the application level. This covers the full translation of biological discovery, preclinical validation in experimental models to human data, and backward for bringing new solutions for disease challenges, identifying current and future unmet needs and possible solutions to overcome these. The goal of translational medicine is to help patients with the more rapid development of new solutions at the diagnostic and therapy level, facilitating new health care interventions for unmet clinical needs. In this context, massive evidence suggests that the process, long and complex by nature, requires strategic planning when a biological discovery is seen as an opportunity for developing a new health intervention. Projects and initiatives located at the initial steps of this value chain often suffer from lack of understanding of the complexities of efficient translation. As this is, by definition, a multidisciplinary process where science is not the only driver, the lack of strategic perspective in areas such as regulatory science, HTA assessment, data management strategy, Innovation management which result in an increasing difficult journey.

This WP will establish strong links to WP3 and WP4 and all projects funded by ERDERA will be assigned a mentor champion who will identify, if required, additional mentors. Mentoring support will be provided by organizing a meeting (or meetings) with the project team where the development plan will be discussed, and mentor will guide the team on the expected and predicted translational bottlenecks. Also, in this meeting specific gaps which may require additional expertise will be identified. FGB will perform a feasibility study that at the end of Year 3 will report on the potential need for the partnership to establish a workflow for providing additional support based on a consultancy model of expertise support services. This feasibility study will be based on both user experience and mentoring feedback and will also define a potential business model for the long-term sustainability of the service. EATRIS will facilitate FGB contacts with the experts of the EATRIS database and getting their feedback which will be key for the development of a feasibility study on additional consultancy services. This process will be implemented during the initial funding cycle (M1-M36).

Objectives

This activity aims at providing researchers from projects funded by ERDERA with a central Mentoring support service intended to guarantee best chances of success in project execution and ERDERA research activities, as well as subsequent exploitability of the results.

The activities for the AWP Year 1 of WP are to design the workflows and initiate the process for providing mentoring service and assessing the potential inclusion of consultancy-based services, activities based on the specific objectives of WP17:

- Continue and further expand the successful EJP RD mentoring program accompanying WP3 and WP4 funded projects starting at the design phase and if required also during project development. Mentoring teams will provide early support for the design of the development plans followed by a light-touch follow-up during project development.
- Initiating a feasibility study of a potential workflow for additional expert support based on a consultancy service-based model. This study will include a business model analysis for long-term sustainability of this potential service provision. The assessment of this study at the end of Year 3 will be determinant for including this additional workflow during the second funding cycle.

Description of Programmed Activities

T17.1. **Execution of the Mentoring Program (M1-M12)** *TL: EATRIS; Contributors: FGB, VHIR.* T17.1. aligns with GO:1,2; SO:2,4; OO:2.
In Year 1, mentoring activities will be dedicated to the definition and organisation of the program, to the design of the workflow, to the release of a Standard Operation Procedure (SOP), to the identification of the mentors and to the development of training material for mentors including the mentoring handbook. Moreover, the first round of the mentoring program will be run for the 2025 calls (M8-12). EATRIS, as leader of this task, will assign a mentor per each project who will be responsible for the execution of the mentoring process. The mentor champion might identify, if requires, additional mentors. Mentoring support will be provided in a live meeting with the project team where the development plan will be discussed, and mentor will guide the team on the expected and predicted translational bottlenecks. Also, in this meeting specific gaps which may require additional expertise will be identified. During the mentoring activities, the mentor will oversee assessing achievement of milestones and providing advice on further steps to maximise the project's potential of success and further development towards the clinic.

ST17.1.1. Operational workflows *STL: EATRIS Contributors: FGB, VHIR*
The characteristics, workflows and timelines of the mentoring process will be discussed and a specific SOP illustrating the workflow of the program will be created. This workflow will include a Confidential Disclosure Agreement (CDA) template that will be signed by mentors participating in the program. This workflow will be revised, assessed, and validated by the ERDERA coordination team and by other relevant people involved in the activities (e.g., WP leaders, Call Secretariat Coordinators, etc.) at M5. Inputs and comments will be addressed and implemented in the final version of the workflows. At M6, following the finalisation of the SOP and the workflows, a handbook for mentors will be prepared and disseminated across the experts registered in the database. This handbook will include all necessary materials for performing the mentoring activities within the ERDERA, including the templates for reporting individual projects as well as the overall assessment for the mentoring process. At M6 a cycle of webinars and/or video materials and protocols will be produced and made available to discuss with the mentors the processes and timelines that will be executed in 2024.

In preparation for the mentoring process, a specific webinar will be organized with the mentors involved in a particular call to have a direct interaction, solve doubts, and prepare the interaction with the project teams. **The activities to be developed during Year 1 include** (a) the development of the SOPs for the mentoring program and the description of the workflows during M1-M4, (ii) the preparation of different templates that will be used for the task during M1-M4, (iii) meetings with the coordination team to align on the development of the activities (M4 and M7), (iii) the establishment of the workflows for the mentoring process during M6, (iv) the preparation and dissemination of the mentoring handbook describing the whole workflow during M6-M10, (v) specific webinars for the mentors to train them into the mentoring process during M8 and the first round of the mentoring program which it is foreseen at M8-M12.

ST17.1.2. Database of multi-disciplinary experts *STL: EATRIS Contributors: FGB, VHIR*
During the first 3 months of the project, EATRIS will update the mentoring experts' database that has been operating to support the mentoring program of EJP RD. Additional experts will be recruited after discussion with contributing partners. New mentors can be appointed during the course of the partnership according to the project needs. Mentors consenting to participate will provide the updated Curriculum Vitae and their contact details. Mentoring experts will cover the expertise on the entire research and innovation value chain of RD, including, molecular mechanisms, preclinical research workflows, animal and non-animal models, preclinical technologies, clinical trials, regulatory expertise, innovation management, IP and others. The composition of the mentoring panel will be tailor-made to the needs on the project and suggested by the coordination of the WP based on the previous experience on EJP RD. Elements such as confidentiality and conflict of interest, geographic distribution, gender balance, age balance, and others will be considered during the creation of the database and during the whole execution of the Mentoring program. During the first 3 months potential mentors will be identified and recruited and the database will be updated by the end of M6.

ST17.1.3. Maintaining the Innovation Management Toolbox of EJP RD *STL: EATRIS, VHIR*
The Innovation Management Toolbox (IMT) provides RD researchers guided access to over 450 translational medicine resources on RDs. T17.1.3. will future proof the toolbox by i) ensuring the IMT stays up to date and streamlining the curation process ii) maximising user experience for mentors and mentees and iii) reaching new users. **During the AWP Year 1,** EATRIS will maintain and update the tools contained in this resource. During M2-M8 the tools contained in the IMT will be updated and at M10 an internal workshop will be organized to discuss the current capacities of the tool and strategies for its improvement.

T17.2. Consultancy service (M1-M12) *TL: FGB, VHIR ; Contributor: EATRIS.* T17.2. aligns with GO:1,2; SO:4; OO:2.
In Year 1, consultancy activities will be dedicated to the definition of the service, to the design of the workflow, to the identification of the experts and to the release of the fee scheme to the researchers. This will be aimed at exploring the need and the interest of providing additional expert support in the framework of a consultancy-based support service. Direct feedback from the mentoring service, as well as surveys and interviews with RD research teams will be the basis for a feasibility study that will assess the interest of creating a consultancy-based service as an additional workflow in ERDERA activities. This study will analyse the priorities, workflows, and financial sustainability of these potential service provision approaches.

ST17.2.1. Feasibility study to provide consultancy service
A study to assess the feasibility of a model to provide consultancy services will start in Year 1. Such a study will analyse the needs of from the scientific community involved in the RD domain for consultancy support through surveys/interviews to/with the relevant stakeholders, including those from other WPs and groups (EAG, WP18, WP19 and the Data Services Hub). **Then, in Year 1 the following activities will be undertaken:**

- The needs analysis will be performed through surveys and interviews with RD research teams.
- The types and contents of consultancy services to be offered will be identified.
- The dentification and mapping of expert(s) according to the expertise and availability will start, also using the database created within T17.1 and liaising with the dedicated WPs and groups.

ST17.2.2. Pilot conduct
For the second funding cycle, the feasibility of the consultancy model built in this subtask will be tested on some selected projects. This subtask will prepare dissemination materials for informing the community of the initiative.
This activity is not planned in Year 1.

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Additional deliverables *(additional to those included in part B of the proposal)*
None

Set of Activities Number	**18**	**Start Date or Starting Event**			**M1: September 2024**		
Set of Activities Title	**Regulatory support service**						
Short name of participant & (No)	FGB (23)	EATRIS (22)	Pfizer* (161)	AZ* (150)	IABS-EU (134)	RJF (164)*	Miltenyi* (160)
Person Months	20	14	1	2	4.2	3.1	2.4
Short name of participant & (No)	UCB* (167)	ROCHE* (165)	HIPRA* (157)	LAB HIPRA* (158)	FDB* (154)		
Person Months	1	1	2.5	1.3	2.4		
Start month	M1	**End month**	M12				
**Associated partners providing in-kind contribution*							

State of the art behind this WP
ERDERA foresees research activities aimed at supporting and developing promising RD research tools and therapies, such as ATMPs. These tools should be implemented smoothly in a more efficient, patient needs-targeted and less costly development process. Key to achieving these objectives is the compliance with the applicable regulatory provisions, to get greater certainty in their developmental paths, by defining a clear research & development plan, and ensuring the methodologies applied are accepted by regulators. To this aim, regulatory activities should accompany any research from the beginning to its completion and should keep informed by the updates that are continuously released by the regulatory authorities. This should be done by reviewing what is currently available, identifying gaps and by interacting with regulatory agencies and other stakeholders, such as pharmacopoeia. Guidance on addressing regulatory requirements properly should also consider the variability of the regulatory frameworks across countries. Such a variability carries different expectations around the level of control of the safety, quality, and efficacy of these products between the various health authorities. As a result, the need to refer to a harmonized set of rules that represents a major need of the field and as such, a major priority of ERDERA. The development of new therapies for RDs including promising ATMPs is complex, time consuming, expensive, and comes with numerous uncertainties due to the relative immaturity of the technologies employed. Their promise to make a meaningful difference to the treatment of RDs is therefore hampered and seen as commercially unattractive. Central to addressing these issues is the need for consensus on common standards that facilitate more efficient development and the design of more effective, cost-effective clinical studies that are compliant with regulatory requirements.

To facilitate more efficient development of therapies for RD, there is a need for more specific and extensive guidance, quality standards (e.g., monographs) and physical measurement standards covering manufacturing, nonclinical and clinical development. This requires close interaction with regulatory experts, technology developers, clinicians, and patients to define what standardized processes are critical to create a more streamlined, transparent, and cost-effective RD therapy development process for the benefit of patients.

Methodology

The regulatory support service of the ERDERA will be provided by a group of regulatory experts from industry, academia, not-for-profit organisations, patient representatives, and regulators from the public sector, through the immediate establishment of a dedicated regulatory support group to fulfil the regulatory needs of the alliance. Central to this regulatory service will be the establishment of an effective monitoring, assessment, and support process that the ERDERA regulatory support group will implement to provide timely support where and when needed. This will be done in close collaboration with the EAG, Mentoring & Consultancy, CRNs, Data and Accelerator Hubs to ensure all regulatory needs are prioritized and supported. The necessary links will be established accordingly. **During Year 1,** WP18 will ensure that CRN, Data and Accelerator Hub WSs will be helped with sources, guidance, recommendations, and webinars. The Regulatory Support Group will participate in CRN and Accelerator Hub meetings. The group will periodically liaise with the EAG to ensure alignment on the ethical and regulatory strategy and to jointly address requests for support on non-clinical and clinical issues being both ethical and regulatory. The Group will be also in charge of regularly sharing updates of regulatory documents relevant to the EU through the project communication channels.

Objectives

This WP aims to provide beneficiaries with a multi-specialistic regulatory support service, ensuring that consortium-derived tools, methods, data, and sources are in line with up-to-date requirements for regulatory filings including qualification. **Specific objectives for Year 1 are:**

- To create a one-stop point for regulatory scientific questions related to preclinical and clinical research in the form of a dedicated project Regulatory Support Group;
- To start developing new regulatory support tools outlined in T18.1 and T18.2 to facilitate more effective translation of new therapies to the clinic;
- To start operational activities to provide advice on opportunities, strategy, and timings to engage with regulatory agencies at the appropriate time during the project;
- To start operational activities to facilitate the applications for regulatory procedures to the European Medicines Agency (EMA) or other regulatory bodies, e.g. National Competent Authorities, including the qualification of novel methodologies and standards to streamline new therapeutic development for RD;
- To provide the necessary guidance required to support efficient, regulatory-compliant first in man clinical trials.

Regulatory support, both for clinical and non-clinical research, will be also delivered to researchers from funded projects through consultancy services (T17.2).

Description of Programmed Activities

A Regulatory Support Group will be created within the first 3 months of the project. This expert group will consist of representatives from industry partners, academia, not-for profit organizations, patient representatives, and regulators from the public sector with extensive knowledge of regulatory science around devices and medicines development for RDs including ATMPs. The regulatory support group will provide CRNs, Data and Accelerator Hubs with the sources, guidance, recommendations, and webinars they need, to facilitate the advancement of their objectives through regulatory compliant processes. The Regulatory Support Group (RSG) will periodically liaise with the EAG to ensure alignment on the ethical and regulatory strategy and to jointly address requests for support on non-clinical and clinical issues including both ethical and regulatory support for clinical and non-clinical research. This support will also be delivered to researchers from funded projects through consultancy

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services (T17.2). Through these activities, this WP will serve to ensure a more efficient, patient needs-targeted and less costly development process for smooth clinical implementation of these must have products for RD.

To achieve the objectives of the WP, the necessary links will need to be established with Mentoring & Consultancy, Data Hub, EAG, and Accelerator Hub within the first months of the projects. To achieve this, an appropriate monitor, assess and support process that the RSG will implement throughout the project will be the main priority of the WP within the first months of the project. This will involve the identification of the right dedicated experts being assigned on case-by-case basis to the different demands of the different projects that require regulatory support. This can include internal demands such as the prioritization/qualification process for newly validated technologies in WP21, to projects demanding clinical support around a CTA application coming in through the consultancy task in WP17. **In Year 1,** priority will be given to the establishment of procedures to regularly share updates of relevant regulatory documents for the EU through the project communication channels.

T18.1. Regulatory support to preclinical research (M1-M12) *TL: EATRIS, IABS-EU, Miltenyi*; Contributors: Pfizer*, RJF*, AZ*, UCB*, HIPRA*, LAB HIPRA*, ROCHE*, FDB**. T18.1. aligns with GO:2; SO:1,2,4,5; OO:2-5.
Following the establishment of the ERDERA Regulatory Support Group, our first action will be to implement a process to ensure alliance-derived tools, methods, data, and guidelines are in line with regulatory recommendations for regulatory filings. This will include an identification and prioritization process within the regulatory support group to facilitate the qualification of new methodologies developed within WP21 through the creation of appropriate regulatory teams to facilitate different projects. A first assessment will also be carried out in **Year 1** of current Pharmacopeia chapters and monographs related specifically to ATMPs for RDs for relevance and need for improvement and to begin the process of categorizing updates where appropriate. In parallel with this, a first review and round of relevant updates of the EATRIS Regulatory Database (free of charge) with the latest resources for ATMP development for RDs will be implemented. This database will contain information about the regulatory requirements, guidelines, and legislations from 27 EU countries (as well as Norway, Iceland, Liechtenstein, Switzerland, Turkey, and Israel) regarding drug and medical device development derived from the application of European legislation. A dedicated team lead by IABS will start the process to identify the need for new platform standards e.g., analytical method calibrators and written quality standards for raw materials, analytical reagents, and analytical methods will be developed and first priorities agreed on. Based on priority and suitability of any existing standards, the feasibility of realizing these will be determined, and a strategy developed to identify and publish within the project lifespan.

T18.2. Regulatory support to clinical research (M1-M12) *TL: FGB; AZ*; Contributors: TEDDY.* T18.2. aligns with GO:2; SO:1,2,4,5; OO:2-5.
The Regulatory Support Group will advise on regulatory requirements with clinical research and regulatory procedures. This support will encompass different types of clinical studies (clinical studies with medicines – phase I-IV trials and observational - and non-pharmacological clinical studies collecting prospective/retrospective data, including registries, RWD and clinical studies with medical devices) and regulatory procedures (Orphan Designation, Paediatric Investigation Plan, Scientific Advice/Protocol Assistance including the qualification procedures for innovative methodologies e.g., biomarkers, endpoints, registries, patient-reported outcomes, clinical outcome assessments, tools for data measurement/management etc). The research specificities will be addressed: paediatric provisions across all paediatric age groups in case of paediatric studies (informed assent, ad hoc endpoints and procedures, ability to collect samples from children, measures for managing and storing biological samples and associated data, need for paediatric formulations, etc), provisions for genetic tests (specific aims and endpoints, informed consent and recruitment procedures), clinical studies with ATMPs according to Reg. 1394/2007/EC.

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To this aim, the Regulatory Support Group with specific expertise in clinical research will start focusing on the topics that need to be covered. It will set and prioritise liaison with the CRNs, to identify the areas where specific regulatory support will be needed. The necessary links will be also established with other project groups and WPs:

- The EAG, to ensure regulatory- and ethically compliant research and data collection and the proper alignment on the issues being both ethical and regulatory e.g. Informed consent/assent, processing of data in line with GDPR and related guidelines, handling biosamples, implementation of provisions from GCP, Regulation (EU) 536/2914 in case of CTs with medicines, and from the EC Recommendations in case of paediatric studies. This effort will be also reflected in updating the consortium on applicable provisions.
- The Data Hub, to ensure that data and knowledge produced in projects meet the standards of the regulatory process.
- The Consultancy service, to suggest regulatory experts to be involved in consultancy requests.
- The Methodological Support WP, to discuss the possibility to undertake the Qualification Procedure for the innovative methodologies. This will also consider the need from CRNs to implement regulatory-compliant innovative methodologies in their clinical research;

This will be preparatory to set up the sources, guidance, recommendations and webinars on the use of data and samples collected during both routine care and clinical studies for regulatory purposes, e.g. dossiers for marketing authorisation applications of medicines and medical devices, clinical studies. Other aspects will be addressed based on the beneficiaries' needs. To this aim, the FGB Regulatory Database will be updated. At the end of the Year 1, the workshop with regulatory experts on regulatory challenges in the RD domain will be held and the first outputs of the group will be shared with the consortium.

ST18.2.1. Clinical studies, data, and samples handling

The Regulatory Support Group will deal with the regulatory aspects of clinical studies, prospective and retrospective processing of health and genetic data and biosamples handling. **In Year 1**, the group will set up the necessary actions to allow the proper support to:

- Advice on the proper regulatory definition and classification of clinical studies and consequently on the documents to be prepared for their application to the competent bodies, i.e. Regulatory authorities and ethics committees.
- Perform the regulatory review of clinical study protocols (T10.2) and related documents, addressing research specificities (stated above).
- Advice on the regulatory-compliant use of samples previously collected in the context of routine care, as well as new of samples allowing their use for regulatory purposes.
- Allow a regulatory-sounded processing of data in line with the European general data protection regulation (GDPR) reg. (eu) 2016/679 and its compliance in third countries.

This will accompany the CRN from the beginning of the project.

ST18.2.2. Engagement with regulatory agencies

The Regulatory Support Group will facilitate engagement with regulatory agencies, including the European Medicines Agency (EMA), to receive the proper support/advice. In order to help identifying the most suitable regulatory procedures where the research activities need to be included, preparatory activities will start in **Year 1** of the project to facilitate the liaison with the relevant regulatory agency and support their preparation and application. Whenever relevant, other regulatory agencies/authorities will be addressed as well, e.g. as the EU national competent authorities, Food and Drug Administration (FDA) and Japanese Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA).

Additional deliverables *(additional to those included in part B of the proposal)*

None

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Set of Activities Number	**19**	**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Methodological support**					
Short name of participant & (No)	APHP (24)	UHASSELT (25)	UKA (114)	INSERM (1)	PLUS (141)	UU (121)	SFU (99)
Person Months	12	12	4	4	4	4	1.8
Start month	M1		**End month**	M12			

State of the art behind this WP

Over the recent decade, the beneficial role of the use of adequate design and analysis methodology for empirical studies (CTs, RWD, registries), tailored to the needs of RDs has become apparent, through projects as IDeAl, ASTERIX, InSPiRe, the EJP RD demonstration and innovation projects, and beyond. The EJP RD capitalized indeed on these previous EU projects and initiated a double process to accelerate the implementation and validation of adapted methodologies for clinical trials in RD:

- Accelerating the demonstration of the usefulness and feasibility of the small sample methodologies developed previously for use in RDs.
- Initiating innovation projects for key unmet needs in clinical studies in RDs. This rich background enabled the building of a group of excellence in methodologies for clinical studies (CS) encompassing a large spectrum of expertise and highly informed about the specific needs of patients, researchers, and clinicians to achieve successful CS.

Methodology

This WP places itself in the tradition outlined in the State-of-the-Art. It will build on the methodological collaborative tradition of IDeAL, ASTERIX, InSPiRe, and the EJP RD achievements.

Major challenges are the use of appropriate methodology in the context of RDs, where the information available per subject may be large, but the number of subjects is typically small. The complex nature of the data takes the following form: data tend to be multivariate, potentially with outcomes of different data types, measures longitudinally, subject to other hierarchies in the data (e.g., coming from meta-analysis or multi-stage sampling designs), and are generally prone to incompleteness. Against this background, methodology needs to be applied that is statistically adequate (i.e., as precise and unbiased as possible), as well as computationally feasible. Further, it is imperative to ensure proper integration of CT and RWD, such as epidemiological studies and registry data. Apart from likelihood and Bayesian methodology, we will consider randomization-based methods, as well as methods based on generalized pairwise comparisons.

A challenge is the efficient transfer to the clinical field, i.e., to the CRNs and other health care centres throughout the European Union where clinical trials and other empirical studies are conducted. To this aim, liaison with the Regulatory Support Group will be established to discuss the possibility to undertake the EMA Qualification Procedures for the innovative methodologies developed within WP19.

Objectives

This WP will contribute to the knowledge transfer of (bio)statistical, data scientific, epidemiological, AI, and machine learning expertise with the CRNs and other partners. The emphasis is on clinical trials, epidemiological studies, registries, RWD, and combinations thereof. This rests on State-of-the-Art methodology and its implementation. If needed, when the clinical trial topics have been consolidated, methodology will be further refined and updated. We will contribute to the consultancy services related with research methodology, as mentioned in WP17. A strong interaction will be foreseen with the WP Data Readiness, the WP RWD, the WP Finding and Accessing the Data Ecosystem, the WP Data Readiness Services, the WP Data Sharing and Analysis Services and the Regulatory Support Group.

The objectives for Year 1 are:

- To initiate the methodological knowledge transfer, whereby at least one concrete (clinical) case will be identified.
- A review will be started regarding methods available for the use of RWD, useful to the context of RDs. The partners to work on this objective will be identified. This will lead to a draft report, to be expanded, improved, and fine-tuned in subsequent years.
- A review will be started regarding methodology for RDs design and analysis, when data are hierarchical, incomplete, and/or of different data types. The implementation of these methods in a user-friendly software library will be initiated. This will lead to a draft report, to be expanded, improved, and fine-tuned in subsequent years.
- A review on the existing methodology of a non-parametric, pharmacometrics, and randomization-based nature will be initiated. This will lead to a draft report, to be expanded, improved, and fine-tuned in subsequent years.

Description of Programmed Activities

T19.1. Methodological knowledge transfer towards local clinical trial teams (M1-M12) *TL: APHP, INSERM_U1138, SFU; Contributors: UHASSELT, UKA.* T19.1. aligns with GO:2; SO:1,2,4,5; OO:2,3.
Only few experts are proposing and applying innovative CT designs tailored to small sample sizes, as is common in RDs. Often, clinical trial units in the field do not dispose of adequate knowledge or experts to plan clinical trials using designs specifically developed in the context of RDs (tailored to patient's heterogeneity, small sample setting, non-standard endpoints, etc.). This is why this WP's team will propose knowledge transfer in terms of (1) proposing suitable designs for RD clinical questions, (2) providing help in the protocol writing, (3) discussing computational code or statistical package, (4) providing support during the conduct of the trial and in the trial analysis, and (5) participating to the scientific manuscript writing. The idea is not to replace the work of the local teams but to transfer the expert's knowledge, tools, and confidence as a learning process. Local teams should be able to use the first trial as an opportunity to develop new skills to be used in future studies. Nabbout, Molenberghs, and Hilgers have a long tradition of collaboration, in the RD context, and will closely work with Zohar and Heussen to identify the precise knowledge that is needed and jointly organize the transfer to the local teams. **Specific tasks for Year 1:** The methodological knowledge transfer will be initiated. At least one concrete case will be selected, the methodological needs identified, and the transfer process initiated.

T19.2. Novel methodology for the use of all available knowledge, including RWD (M1-M12) *TL: INSERM_1138, UHASSELT, APHP; Contributors: PLUS.* T19.2. aligns with GO:2; SO:1,2,4,5; OO:2-5.
To better characterize and understand patient's disease trajectories and treatments, in RDs, one would need to use multiple data sources coming from patients (i.e., Real World Data, registries, clinical trial data, etc.) and preclinical trial findings on the disease pathway and mechanism. Patient reported outcomes are evidently part of the data biotope. Incorporating this knowledge into the design of a clinical trial or RWE is not straightforward and it requires specific methodological considerations. This

WP's team will propose statistical and machine learning approaches to maximize the use of existing knowledge. We will propose multi-modal approaches, allowing modelling and analysing multi-source (preclinical and clinical) and multidimensional (omics, etc.) data. This will be in support of the Data Hub and every WP involved with the design, conduct, and analysis of clinical trials. INSERM and UHasselt partners have partially complementary bases of knowledge and expertise. T19.2 leaders will identify partners within their organizations, as well as within organizations of the other partners in this WP, who are most appropriate for a given study. If necessary, they will identify which additional work needs to be done to expand the methodological toolbox further. The benefit of this WP will be richer, more informative clinical trials in RD, benefiting the clinical trialists, the funders, and evidently and foremost the patients. **Specific tasks for Year 1:** A review of methods for the use of RWD, useful for the context of RDs, will be initiated; partners to work on this problem will be identified. A concrete use case will be identified, to initiate the tailoring of methodology to this task.

T19.3. Data analysis methodology when data are multivariate, hierarchical, incomplete, and of differing data types (M1-M12) *TL: UHASSELT, PLUS, APHP; Contributors: UU.* T19.3. aligns with GO:1,2; SO:1,4,5; OO:2-5.
Analysis of CTs in RD ideally makes use of all data available. This includes the simultaneous analysis of data of differing types (time to event, continuous, count, binary, categorical, etc.). CT data will be supplemented with data from other sources. Each of these outcomes with its specific modelling tools, but also its challenges. These challenges exacerbate when data are collected longitudinally. At the same time, longitudinal data offer a rich but often undervalued data source. For example, a single value of a marker may be of little or no use, but its evolution over time may be extremely indicative. It is more and more common for multiple outcomes to be measured longitudinally. The joint analysis of multivariate longitudinal data requires specific statistical knowledge, both in terms of modelling and data analysis on the one hand, as well as in computational terms on the other. Indeed, when multiple sequences are modelled, classical fitting methods, such as maximum likelihood and Bayesian estimation may break down. This is true in general, but especially in small samples, common in RD, because then there is a different balance between the sample size and the complexity of the data structure. The combined knowledge of the modelers (who developed, among other tools, pseudo-likelihood, or computer-intensive tools), experts in generalized pairwise comparisons, and randomization-based inference is of great value and will allow a unique set of solutions that are highly relevant for the rare-diseases community. Their transfer is essential, potentially upon fine-tuning to the need of the RD data stream (CT, Real World Data, registry, or a combination thereof). Regarding the adequate handling of missing data, the primary analysis strategy should be chosen carefully and conventionally so that the assumption of Missingness at Random applies. Then, sensitivity analyses should be done to investigate the stability of the results. This has set in motion an entirely new strand of currently ongoing research, ranging from new modelling strategies for incomplete data (e.g., based on multiple imputation), over sensitivity analysis, to computational strategies. A very elaborate machinery exists to evaluate surrogate endpoints in CTs. The use of a surrogate, or multiple surrogates, in lieu of the usual clinical endpoint can increase information and time. Whereas in common diseases it allows to reduce sample size, in the RD context it can ensure that the maximally available sample size provides enough information to test a clinically meaningful hypothesis. The partners have interacted closely in developing and making available methodology through IDeAl and EJP RD; they are thoroughly familiar with each other's expertise and will bring it together to optimally advise on methodology or, should it be needed, to expand the toolbox further. The benefit of this methodological WP is to the clinical trialist (design, conduct, analysis), the funder, and the patient. **Specific tasks for Year 1:** A review of the methods associated with this task will be undertaken and written such that it is useful to methodologists, trialists, clinicians, and other stakeholders. Preparations will be made to (re-)implemented these methods in a user-friendly software library. Development of novel methodology, building on existing one, is foreseen for AWY2 and later.

T19.4. Non-parametric, pharmacometrics and randomization-based methodology (M1-M12) *TL: UKA, UU, APHP; Contributors: PLUS, UHASSELT.* T19.4. aligns with GO:2; SO:1,2,4,5; OO:2,3.

Methods such as generalized pairwise comparisons have been developed for multiple outcomes, either when a hierarchy in the outcomes is present, or when this is not the case. Their place in the context of RDs should be carefully considered. On the one hand, they are computationally convenient, on the other, their power properties need to be examined for a given trial, such as considered within a CRN. Simulation based evaluation, tailored to the needs of a specific research question, in the context of a specific RD, should be undertaken. Pharmacometric models based on nonlinear mixed effects analysis of longitudinal data are particularly suitable for RD, given their ability of making use of all relevant data in a structure that allows the use of prior information. **Specific tasks for Year 1:** The existing methodology, on which this task builds, will be reviewed, and brought together in an accessible text. An overview will be made of available software. The gaps and extensions needed will be identified. Filling these gaps and preparing these extensions is foreseen for Year 2 and later.
Additional deliverables *(additional to those included in part B of the proposal)*
None

Set of Activities Number	**20**		**Start Date or Starting Event**			**M1: September 2024**	
Set of Activities Title	**Education and Training on RD Research**						
Short name of participant & (No)	EURORDIS (26)	VULSK (27)	WDO (120)	DDF (51)	GA UK * (168)	TEDDY (105)	c4c-s (122)
Person Months	21.4	14	3	2	1.2	2	3.4
Short name of participant & (No)	IMAGINE (70)	ASU-FC (39)	CNAG (10)	FFRD (29)	SRUMC (11)	UT (8)	UTARTU (9)
Person Months	1	7	6.9	2	2.5	2	0.5
Short name of participant & (No)	TUM (12)	Fraunhofer UK* (167)	EATRIS (22)	ECRIN (57)	UHASSELT (25)	ISS (75)	
Person Months	0.5	1	3	1.5	1	3	
Short name of Participant & (No)	UMCG (19)	LUMC (16)	AUMC (20)	UTWENTE (17)	SFU (99)	UCSC (112)	ACU (35)
Person Months	0.5	0.5	0.5	0.5	6,9	5.2	1
Short name of participant & (No)	UCD (111)	SU (142)	RSU (96)	IBG (68)	ISCIII (72)		
Person Months	1	0.5	0.5	4.2	1		
Start month	M1		**End month**		M12		
**Associated partners providing in-kind contribution*							
State of the art behind this WP							
Education and training on RD research are among the highest priorities to empower the entire RD research community to tackle RD-associated challenges and to bring the real value to PLWRD. In							

recent years, many educational resources have been developed incl. not only the comprehensive EJP RD training programme but also ERICA resources, the ERN Knowledge Academy, etc. Those resources need further dissemination and awareness raising to be adopted by the national systems and/or various communities of stakeholders. This will be fostered through ERDERA WP2. However, severe gaps remain in the overall landscape of RD research education and training and novel needs constantly arise due to unprecedented progress in the field. These needs must be constantly monitored, identified and fulfilled across many axes (including career stages, multistakeholder community needs, regional needs, research and innovation developments). Covering the entire RD research ecosystem, ERDERA has exceptional opportunities to identify and meet these needs, high added value brought by European and international collaboration and measures for long-term sustainability of developed resources. In the overall RD research community, ERDERA may act as a direct provider, major contributor and collaborator in education and training activities and ensure advisory role for policy/ decision making.

Methodology

The main streams underlying the organization of education and training contents have been identified according to the expertise level and cover the entire RD research multistakeholder community according to the principle of pyramid. Training has been thematically organized to empower multistakeholder communities in ERDERA activities as a priority. As such, trainings will empower:

- RD diagnostic research and RD clinical research (for participation in WS CRNs, WS RD funding);
- Knowledge on research methodologies (WS Expertise services Hub, WS RD Funding);
- Translation of research and CTs (WS CRNs and WS Acceleration Hub);
- Data research (WS Data services Hub, WS RD funding).

The overall RD education and training landscape encompass many education and training providers (including universities, medical and nursing schools and their associations, professional organizations, ERNs, patient organizations, research institutions and infrastructures as ESFRI). All together, they implement the four main aims of education and training in RDs and rare cancers 1) to ensure efficient timely diagnosis; 2) to ensure efficient, integrated, coordinated, multidisciplinary specific and symptomatic care; 3) to empower patients; and 4) to foster research. Sharing responsibilities among all education and training providers in the most efficient and effective way is of utmost importance as well as complementing without duplicating the efforts. Having this concept in mind, the ERDERA comprehensive and coherent education and training programme was set up to:

- Provide education and training on RD research (as opposed to medical education and training that should be provided by the medical schools, universities, teaching hospitals and ERNs);
- Target mostly general overarching needs in RD research (as opposed to trainings on individual RD or groups of RD, although teaching on the latter may be encompassed as case studies and examples);
- Target mostly highly-specialized expert-level and intermediary level of expertise, in one common language, English (as opposed to the basic, general teaching on RD concepts that has to be provided to all medical and life sciences students, clinicians and other stakeholder groups at the base of the educational pyramid, most frequently – through the formal educational programmes and in national languages, i.e., mostly beyond the scopes of ERDERA).

Strategic alignment for this responsibility sharing in RD education and training will be ensured through the activities of ST20.2 with a constant monitoring of the state-of-the-art of RD education and training and liaison with internal (all ERDERA workstreams) and external stakeholders (in collaboration with WP25). Moreover, as a global and European initiative, ERDERA has exceptional opportunities that would be impossible to achieve by other means and a very high added value of collaboration, including:

- Timely identification and fulfilment of training needs, gaps and arising novel needs through the tight interaction with all ERDERA workstreams and embedment in the overall RD research

ecosystem. These are of especially high consideration for the highly innovative areas and trends where educational programmes and resources do not exist and for the highly specialized topics where educators and learners are as rare as RDs themselves, hence, there is a limited scope for the development of national educational programmes and international collaboration is a prerequisite;

- Onboarding of the most knowledgeable and experienced education and training providers, including those based on the European collaboration (as ESFRI), to ensure not only high quality of education and training but also sustainability of the resources that will be developed in ERDERA;
- A set of measures for a wide dissemination of high-quality trainings including: i) engagement of international multistakeholder faculties for the development of education and training that sets the stage for sharing of developed resources; ii) wide geographical coverage of trainings through, e.g., course rotation; iii) gradual and scaled approach to the trainings according to the learner's level of expertise from more basic training (that involves large numbers of learners) to advanced, expert-level training (that is more demanding in terms of resources and involves smaller numbers of selected, highly-motivated learners); iv) adequate age- and career-stage appropriate methodology of education and training to the targeted audiences and specific/local needs; v) development of open, shareable educational resources and on-line trainings for a wide outreach; vi) application of train-the-trainer principle in collaboration with WS Inter(National) Capacity Alignment that enables identification and fulfilment of individual national needs and wide dissemination of the benefits of ERDERA education and training programme towards national systems (explained in more detail below); vii) leveraging on a wide RD research ecosystem of ERDERA for the awareness-raising of newly developed and existing education and training resources in collaboration with WP2;
- Application of specific measures to increase participation of underserved groups and learners from underrepresented countries (as fellowships for training courses) that, together with the specific measures applied in other ERDERA workstreams (WS Research Funding and WS Inter(national) Capacity Alignment) create a comprehensive, coherent programme for inclusion. Strategic and practical sustainability will be achieved through the development of trainings by established organizations and networks, standardized adaptation of training contents according to the identified needs, dissemination through the train-the-trainer principle to the national systems and/or various communities of stakeholders.

ERDERA is in the exceptional position of empowering one of the usually underserved multistakeholder groups: patients and patient representatives. The main aim of the education stream for patients and researchers (WP20.1) is to build capacities of patients and young researchers and to foster their participation and collaboration in RD research. To achieve the highest possible effectiveness, a blended (on-line and face-to-face training courses) and scalable (from beginners to advanced level) programme is proposed. Promotion of the establishment of university educational programmes for RD researchers and international collaboration of universities in these activities with the final aim of having an interuniversity European diploma will be implemented in WP20.4. A gradual approach is foreseen: first, compilation of a core-set educational modules from different universities, next – short-term pilot programme, then scaling-up to the full curriculum of 60 ECTS. A continuous evaluation and improvement process will be applied. Preliminary selection of educational directions for a coherent, comprehensive ERDERA education and training programme was based on the preliminary investigation of existing resources, investigational work done in the EJPRD and a tight interaction with all ERDERA workstreams with the final aim to empower the learners for participation in all ERDERA activities (including CRN, Acceleration, Data Services hubs and RD funding) and in the RD research activities beyond ERDERA (mostly at national level, through the application of the train-the-trainer principle).

Various age-, career-stage- and topic-appropriate pedagogical tools will be used with the aim of identifying the most effective and efficient ways to deliver education and training contents (F2F or on-line trainings, expert-level horizon-scanning webinars or hands-on and problem-based, blended

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teaching, play to learn, etc.). ERDERA education and training providers will comprise a coherent community and will share best practices (e.g., on the adequate pedagogical methods, procedures for the selection of highly motivated learners or effective awareness-raising ways) and resources (e.g., forms for registration, evaluation of applications, feedback collection forms, programme forms, practical approaches including play to learn method, etc.).

Objectives

The main objective of WP20 is to develop a comprehensive programme of education and training on RD research that serves the needs of the RD community across career stages, research, and innovation pipeline and multistakeholder communities.

Specific objectives for Year 1 are to:

- Empower first cohorts of patient representatives (including paediatric patients) to enable their full-scale involvement into RD research for patient-centricity (T20.1).
- Support the RD-focused career development of young researchers (T20.1) through mutual learning with patient representatives.
- Build the foundations of a European University Diploma on RD research (T20.4).
- Identify and reassess training needs to plan the next round of trainings for the following years through the engagement of top-level experts and tight interaction with all ERDERA workstreams (T20.2).
- Develop a first set of online and face-to-face trainings for the RD community following 5 main training tracks: diagnostic research, clinical research, research methodologies, CTs and management, data research. This would enable the RD community to adequately participate to ERDERA activities (Funding schemes, CRNs, Acceleration and Data Services Hubs) and beyond (T20.3).
- Team up with WP2, WP23, WP24 to enable a wide dissemination of education and training to be developed in **Year 1** into national systems through the train-the-trainer principle (T20.2 and T20.3 in conjunction with WP2)

T20.1. Patients and young researchers' trainings (M1-M12) *TL: EURORDIS; Contributors: WDO, DDF, GA UK, c4c-S, TEDDY, IMAGINE, LUMC.* T20.1. aligns with GO:3; SO:3,4; OO:1,3,4.

ST20.1.1. Blended and scalable training programme for patients and researchers across the whole RD research pipeline (M1-M12) *STL: EURORDIS; Contributors: LUMC, WDO, DDF, GA UK*.* The overall objective of this ST is to address one key component of ERDERA to improve research and innovation and to enhance the uptake of research results by building the capacity of the patients and young researchers. The proposed training approach and programme will be developed in recognition of patients' and young researchers' needs (PhD, Post-Docs) for support to be educated on the fundamentals of research in addition to drug development to express their needs, expectations and more importantly aspirations in the most knowledgeable and meaningful way. Training topics will be aligned with ERDERA needs and with the CRN needs as the engagement of expert patients in the CRNs will be of utmost importance. The training methodology approach will foster a blended approach (online and face-to-face). It will be a scalable approach of training patients and young researchers through a 3-step programme: beginner level, intermediate level, advanced level. A strong emphasis will be put on mutual learning among patients and researchers as well as on soft skills that could be further disseminated amongst patient organisations and research labs and organisations. The specific objectives of this task are to equip patients, patient representatives, and young researchers with:

- An understanding of the clinical research, therapeutic development, and regulatory processes for medicinal products.
- The knowledge and skills required for patients to become legitimate collaborators in RD research (from early-stage research to later stages) hence enabling the implementation of the ERDERA strategy supported by the education of patients as well as mutual learning among patients and researchers.
- The skills and knowledge to be empowered as equal, valued, and efficient partners in research and scientific projects as well as all ERDERA activities involving patients.

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The training programme will be organized in 3 levels. **In Year 1,** all 3 steps will kick start and be held once each.

Level 1: Beginner level. This "onboarding research" and basic training will be open to anyone, with no restriction of numbers to be trained (goal: to train at least 2-3000 people a year): patients, patient representatives, researchers. Connection with WP2-Communication & dissemination, WP23-NMGs promotion and national alignment and WP24-Fostering engagement of underrepresented countries will be ensured so that the EURORDIS Open Academy (OA) online resources can be further disseminated and more widely used. Over the 3 past years, circa 30% of the audience of the OA was from outside EU, with learners coming from more than 150 countries. For this beginner level, with learners on-boarding the RD research ecosystem, no fixed cohort would be formed. The access to the content will be free and on-demand. Learners would be able to sign-up at any time and complete at their own pace. Topics will cover medicines research and development, introduction to the RD research landscape, introduction to EU institutions, advocacy, RD diagnosis, introduction to genetics and genomics, registries, patient partnerships in research, etc. Trainees must complete all basic courses in this category to be eligible to move to the intermediate level.

Level 2: Specialised pathways. Enrolled trainees of the specialized pathways must have completed all basic level training beforehand to qualify. The objective is to train up to 100 people per year. It will be a single application process for patients and young researchers where they select the different pathways to follow (maximum of 35 trainees per pathway). Participants will be able to apply for more than one pathway. A blended format lasting between 6 to 9 months with staggered start of 3/4 pathways: 1) medicines research and development, 2) ethics, 3) diagnostics, 4) building patient partnerships in RD research, etc. A 3 day-training workshop will be hosted at the end of the training, with practical exercises and topics on cross-cutting issues. Partnerships are foreseen with European research institutes and universities to organise and increase the mutual learning between researchers and patient representatives.

Level 3: Advanced level. Completing an intermediate level training (see above) will provide the eligibility to participate in an advanced level training. Specialized topics will be covered such as PROMs, new orphan drug regulation, data and digital latest innovation, etc. All topics and training needs will be continuously reassessed based on the needs fed back by the other ERDERA tracks, in particular the CRNs so that the knowledge delivered can directly impact the course of the other tracks. The format will essentially be online, with interactive webinars and no in-person sessions. Signposting of additional courses delivered in T20.3 and from other relevant initiatives and programmes will also be done on a systematic basis. Having completed the advanced level programme will give access to a personalised follow-up or a mentoring programme to an approximate number of 20 patients/patient representatives a year. They will be selected following a specific application process.

ST20.1.2. Training workshops for paediatric patients (M1-M12) *STL: TEDDY; Contributors: c4c-S, IMAGINE, EURORDIS.*

This ST will consist in developing a yearly age-tailored training for young people (12-18 years old) focusing on the following areas: (1) rare and genetic diseases specificities; (2) patients' and children rights; (3) clinical and translational research challenges for paediatric patients and relevance of their role (ethical and legal issues); (4) patients' engagement in CTs, participation in CTs and other studies (such as innovative, PROMs, PREMs, etc.); the consent/assent issues, innovative therapies in the context of paediatric RDs, paediatric lay summaries, etc); and (5) Orphan Medicinal Products availability and access for paediatric patients on the EU market, pharmacovigilance and off-label use in paediatric setting. **In Year 1,** a first face-to-face paediatric patient expert training will be organised by TEDDY as a 2-to-3-day training course, targeting up to 15-20 young RD patients (12-18 years old). Patients' organisations and YPAGs across Europe will participate in the process by supporting the dissemination of the training opportunity. An online pre-test will be administered to the selected participants to check their knowledge level and interest in healthcare and research fields. This information will allow them to adapt the training plan and activities according to the specific training needs, expectations, and interests of the trainees. In Yar 1 of the programme, the training course will be organised by TEDDY with the support of the other partners involved alongside the support of other networks (e.g., iCAN (International Children's Advisory Network). The training course will be

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performed in English. All contents will be made available to the NMGs to be translated and adapted into national languages (in collaboration with WP23). Training activities will be delivered by paediatricians, investigators, psychologists, representatives of patients' association, YPAGs facilitators, legal, ethical, and regulatory experts, etc. *Ad-hoc* children tailored training materials and tools, to be delivered during the in-person course, will be prepared by TEDDY. Child-friendly information and educational materials, webinars, video, mobile apps and serious game, podcasts in age-appropriate lay language will be developed with participatory methodology including trained children. The material will be further published on the ERDERA website. During the course, practical activities (including play-to-learn sessions) and formal lessons will be organised to facilitate the understanding of the topics discussed. At the end of each meeting, short questionnaires will be distributed to assess the trainees' understanding. The training courses will allow paediatric patients with RDs to get the right skills to be involved in research and make a difference in the experimental procedures. They can have an impact in improving communication with the target population and thus supporting planning and executing research as well as brainstorming methods for dissemination of findings. The pool of trained young patients will be invited to participate in future ERDERA activities when relevant. Collaborations will also be foreseen with Foundations in Europe (e.g., Barretstown Children's Charity) to search for synergies and best practices benchmarking.

T20.2. Identification and fulfilment of training needs (M1-M12) *TL: VULSK, ASU-FC; Contributors: EURORDIS, FFRD, UCSC.* T20.2. aligns with GO:3; SO:4; OO:2,3,4.
The main objective of this task is to ensure a continuous process for identifying education and training needs and to create a strong basis for the introduction of new trainings.

ST20.2.1. Continuous identification of training needs *STL: VULSK, ASU-FC; Contributors: EURORDIS, FFRD, UCSC.*
Training needs will be identified on a regular basis, and **during Year 1** using different sources: interaction with all ERDERA workstreams (mostly through the dedicated meetings during the annual General Assembly and other ERDERA meetings/events); interaction with national systems (through NMGs, in collaboration with WP23); interaction with the global RD ecosystem (in collaboration with WP25. Variable methodologies will be used for the collection of needs, including surveys, interviews, satellite workshops in the ERDERA meetings. These needs will be triaged for implementation according to 1) the main target audience and its career-level and 2) maturity of the educational program (i.e., definition of clear educational goals, contents, established audiences and educational methodologies). When educational needs can be met with the help of existing, already developed ERDERA resources, adaptation of the trainings will be discussed with training developers and implemented, if feasible. Other trainings with established educational programmes and a higher level of maturity may also be implemented in the relevant tasks (T20.1 or T20.3) depending on the main target audiences and topics. For existing trainings beyond ERDERA, awareness-raising and dissemination activities will be activated by FFRD in collaboration with WP2 (incl. Inventory of existing educational resources and infographics). A high demand for ERN-related trainings have been expressed in the preliminary discussions in the ERDERA building phase; for these, the ERN Academy platform will be the key: in collaboration with WP2, an inventory index structure across all ERNs to allow a "one stop shop" access to educational materials developed by the ERNs in the past as well as upcoming ones will be created. For novel, arising needs without any existing educational programs and resources, expert-level horizon-scanning trainings will be organized, from Year 2, mainly in the form of webinars or short workshops and implemented in ST20.2.2. National training needs will be further implemented through the train-the-trainer principle (see ST). After Year 3, evaluation of the state-of-the-art of WP20 RD research education and training in ERDERA and beyond will be accomplished to inform further developments in the field.

ST20.2.2. Implementation of novel horizon-scanning trainings (starts M13).

ST20.2.3. Implementation of train-the-trainer principle (starts M13).

T20.3. RD research trainings for multistakeholder communities (M1-M12) *TL: CNAG, VULSK; Contributors: UT, SRUMC, UTARTU, TUM, EATRIS, GA UK*, Fraunhofer UK, ECRIN, SFU, UHASSELT, ISS, LUMC, UMCG, AUMC, WDO, DDF, UTWENTE.* T20.3. aligns with GO:1,2,3; SO:2,3,4,5; OO:2,3,4.
The main objective of this task is to equip the multistakeholder RD research community (researchers, clinicians, patients, etc.) with the knowledge and skills needed for effective participation in ERDERA activities and RD research beyond ERDERA, especially in national systems towards a federated approach. Therefore, STs are arranged to reflect targeted trainings and contributing to the objectives of the main ERDERA WSs. For the maximum effectiveness, a graded approach of scalable trainings will be implemented: more beginner-level, mostly online trainings will be accomplished in **Year 1** (after these trainings, some of the webinar-like materials will be put onto the ERDERA website to ensure wide outreach and a possibility of usage on a constant basis, while the full online courses will be run according to the foreseen structure of trainings and the needs – once per year or 2-3 years – to ensure "live" online interaction and possibility to raise questions). In the subsequent years, training courses for the more advanced levels will be prepared and implemented either face-to-face or online according to the foreseen structure of training courses. To increase the motivation of course participants and to ensure a certain level of experience, participants in advanced courses will be obliged or highly recommended to complete beginner-level courses first. To ensure the maximum flexibility and adaptation of training courses to the ERDERA and external RD research needs, the budget for training in this specific task has been allocated only for the three first years, allowing to re-analyse the needs and to re-distribute the funding to training providers during the second period based on needs and performance of the training courses.

ST20.3.1. Trainings to empower RD diagnostic research *STL: CNAG; Contributors: SRUMC, UT, UTARTU, TUM.*
The objective of these trainings is to equip CRN diagnostic research participants with the full range of knowledge to select patients for RD diagnostic research, collect and submit phenotypic and genomic data, to use appropriate ontologies and ensure FAIRification of data, to analyse and interpret genomic data for re-analysis, to use innovative omics for RD diagnostic research, etc. The main target audience includes researchers, clinicians, laboratory technicians, data analysts – participants of ERDERA CRNs, RD Diagnostic Research. However, multistakeholder composition and interaction, including patient representatives, is indispensable to ensure effective delivery of training. Trainings in ST20.3.1 will be provided in collaboration with the CRN Diagnostic Research Workstream (WP6-8) in conjunction with the Data Services Hub (WP14-15) to facilitate a seamless integration of the CRN Diagnostic framework into national services towards a federated approach. Methodologies to be used include preparatory on-line lectures, webinars and modules supported by face-to-face hands-on and problem-based learning. Several thematic groupings of trainings are currently foreseen (trainings on genome re-analysis; innovative RD diagnostic technologies; solutions for undiagnosed) with possibility of scaling according to the level of expertise along the duration of ERDERA from more basic to advanced levels. **In Year 1,** preparatory online lectures, webinars, and modules will be prepared for two thematic training groups: a) Management of genomic and clinical data for re-analysis and b) Introduction to innovative omics. These preparatory online trainings will be repeated once per year to once per three years to ensure possibilities for "live" interaction and raising of questions. From Year 2, advanced in-person courses for hands-on training for selected participants will be prepared. It is expected to train 30 to 100 trainees per "live" online session and up to 500 trainees/year through permanent access to the webinars on the ERDERA website. e
ST20.3.2. Trainings to empower RD clinical research (M1-M12) *STL: EATRIS; Contributors: GA UK*.*
The main target audience for ST20.3.2 includes researchers, clinicians, laboratory technicians, biobank staff – participants of ERDERA CRNs, RD Clinical Research. However, multistakeholder composition and interaction, including patient representatives, is indispensable to ensure effective delivery of trainings. During preliminary discussions with ERDERA WS leaders and after evaluation of the maturity of the educational programme, training on cell and gene therapies has been identified as a

priority for the **Year 1**. Other educational programmes may be developed in subsequent years as described in T20.2.

- **Training *"Cell & gene therapy development"*** *TL: EATRIS; Contributor: GA UK.* The training addresses the 4 key challenges and bottlenecks of the ATMP development cycle that prevent new therapies from reaching patients: Scientific & Clinical, Manufacturing, Regulatory, and HTA & Reimbursement. The main audience will be professionals involved in ATMP development from academic research, SMEs, clinics, and regulatory agencies. The methodology will foster a blended teaching approach with preparatory e-learning for more beginner-level participants in Year 1 with advanced face-to-face course (including lectures and hands-on assignment) subsequently. The expected number of trainees is up to 500 participants per year for preparatory e-learning and 30 participants per advanced course from Year 2. Conditions for train-the-trainer principle would be: EATRIS is committed to maximizing the impact and reach of its training. The e-learning will be available for free and can be used as preparatory e-learning by other trainers. National training providers are also welcome to attend the face-to-face course as observers to support the roll-out of the course (e.g., by offering nationally in the local language). r

ST20.3.3. Trainings to empower knowledge on research methodologies *STL: VULSK-Contributors: Fraunhofer UK*.*

The main target audience for the trainings of ST20.3.3 includes researchers and RD multistakeholder community, potential participants of ERDERA funding schemes, from young researchers to experienced principal investigators, and users of the WS Expertise Services Hub. During preliminary discussions with ERDERA WS leaders and after evaluation of the maturity of the educational programme, training on stem cells has been identified as a priority for Year 1. Other educational programmes will be developed in subsequent years as described in T20.2.

- **Training "*Best practice for successful iPSC research"*** *TL: Fraunhofer UK.* The objective of the training is to provide an iPSC training program which covers the entire process flow from consent, legal, quality control, nomenclature and sustainability of cells and data, ensuring that iPSC researchers generating new iPSC line cohorts avoid common challenges and are able to widely share cells and data, increasing reproducibility and access to critical, and often hard to come by RD research tools. The target audience of the training includes all clinical and fundamental researchers using iPSCs, from beginner-level to senior investigators, aiming to inform both the individuals performing the work, and those planning and guiding it. Biobank managers would also be encouraged to attend, as they may hold biospecimen that could be used for iPSC generation or may be in the process of accepting iPSC lines for banking. **The methodology starting from Year 1,** beginner-level training will be developed and provided online. National training courses, according to the selection of countries (to be performed in collaboration with WP23) will be adapted and provided face-to-face in subsequent years. The expected number of trainees is around 30 participants for "live" online sessions of beginner-level training, with up to 100-300 participants/year for continuous accessible webinars on ERDERA website. Conditions for train-the-trainer principle would be Candidates for the 'Train the trainers' program would have to possess some previous experience in iPSCs in some respect, plus they should be familiar with the content of the basic training. For national training courses, we propose a separate module focusing on how they deal with iPSC (ELSI) in their own countries, in practice. This should be face-to-face to enable discussion of specific and/or national issues and ways to overcome them and will inform development of a final, overarching best practice document taking into consideration issues raised. This document can be shared across ERDERA to enable knowledge spreading. o

ST20.3.4. Trainings to empower acceleration of research and RD clinical trial methodologies and management *STL: VULSK; Contributors: ECRIN, SFU, UHASSELT.*

The main target audience for the trainings of ST20.3.4 includes researchers, clinicians, biostatisticians and multistakeholder community, potential participants of CTs, incl. WS CRNs, and users of WS Acceleration Hub. During preliminary discussions with ERDERA WS leaders and after evaluation of the maturity of the proposed educational programme, **training on clinical studies has been identified as a priority for the Year 1.** Other programmes may be developed in subsequent years as described

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in T20.2. Two main groupings of trainings will be implemented: i) Evidence synthesis for clinical studies (biostatistical knowledge) that will be fully implemented in Year 2 and ii) **Management of multinational CTs with Introductory online more beginner-level courses available in Year 1** and upscaling/ adaptation for national trainings developed subsequently.

- **Training "*Evidence synthesis for clinical studies"*** *TL: SFU; Contributors: UHASSELT.* The objective of the training is to provide biostatistical knowledge about study design and related analysis. The main audience consists of medical doctors, nurses, biologists/biotechnologists. The methodology will follow a blended learning approach with a Moodle self-learning platform with face-to-face workshops as well as tandem supervisors. A continuous self-learning preparatory phase with monthly online supervision will be followed by a face-to-face workshop. The expected number of trainees is up to 300 participants per year for the preparatory online webinars and up to 20 participants (split in 5 groups) for the advanced face-to-face course.
- **Training *"Management of multinational trials"*** *TL: ECRIN; Contributors: ECRIN core team and ECRIN EuCos.* This course will be a solution-oriented training course to address the most common barriers in the European landscape. Among the obstacles are the variety of national implementations of the European Regulation on clinical and RD trials that govern European clinical research as well as ethical considerations. The early identification of roles and responsibilities of all stakeholders, in both industry and academic research, as a key aspect to ensure good management of the CT and effective harmonization among participating countries, will be covered. In addition, funding sources and key elements of budget preparation when conducting multinational CTs will be covered, as well as the role of CT data sharing and GDPR when sharing sensitive data across borders. Primary considerations on how to plan clinical research that include data sharing plans, tools and services will be highlighted. The main audience will be principal investigators, sub-investigators, study coordinators and project managers who need training on the management of multinational trials. **The methodology will encompass a preparatory introductory online course in Year 1**, followed by adapted/upscaled advanced courses in different countries, taking advance of the ECRIN distributed organization (see below). The expected number of trainees is up to 500 participants per year for online introductory webinars on ERDERA website and up to 20-30 participants per advanced course from Year 2. Conditions for train-the-trainer principle: ECRIN is a distributed organization working with local experts in the ECRIN member countries, "EuCos", which are clinical research experts in their country, hosted by national partners[18] which are usually CT networks. This structure fits very well with the train-the-trainer principle fostered by ERDERA, as EuCos can contribute both to adapting the training to national specificities and to reaching the relevant audience. This will be implemented through the train-the-trainer principle in collaboration with WP23.

ST20.3.5. Trainings to empower data research *STL: VULSK; Contributors: ISS, LUMC, SRUMC, UMCG, AUMC, WDO, DDF, UTWENTE.*

The main target audience for the trainings of ST20.3.5 includes researchers, clinicians, allied professionals, data managers and multistakeholder community, potential participants of ERDERA funding schemes and users of WS Data Services Hub. The training objectives are to increase the knowledge capacity of RD research stakeholders across Europe on the value of FAIR data and to understand how the framework of FAIR principles ensures that valuable data can be easily found and re-used by different stakeholders to advance RD research. Another training objective will be to efficiently utilize the available legal tools and ethical frameworks accordingly, while considering open science policies, state of the art technologies and upcoming markets, with the focus on data spaces and data intermediaries. FAIR trainings foster future collaborations involving real time and automated analysis of combinations of registries and other types of resources, boosting scientific and regulatory evaluation and healthcare delivery, with the goal to generate open research ecosystems, while empowering digital human rights under the notion of data control rather data ownership. In order to successfully build a "Data Hub" where a higher volume of rich data from several EU patient registries (e.g., PROs), eHealth records, and clinical registries (i.e., post-market data on therapeutics) can be

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combined, the competence and capacity of the RD community to make data FAIR and ready for advanced, trustworthy exploitation must be accelerated. This increased competence will provide added value in answering complex questions effectively, comprehensively, and correctly without moving data from its original source. Trainees will be also upskilled and reskilled towards a trusted and fair data culture, where choices are subject to documented and informed decisions for better research. An integrated training and capacity building programme, developed together with WP14 Data Readiness services and in close collaboration with the WS Data services Hub is needed to support acceleration, encompassing online awareness webinars, in-depth online training with experts, and F2F BYOD' workshops (a combination of hackathon and technical training on FAIR implementation). A new element is competence on preparing data for the regulatory pathway for drug development. Each annual edition is updated with new elements. The training events will contribute to building a solid FAIR ecosystem in the field of RDs. During the trainings ongoing dialogues among stakeholders – clinicians, researchers, regulators/policy makers, companies, patients/families/patient advocacy organizations – will be key and engagement and collaboration between stakeholders can be strengthened. **The methodology: a scaled approach of gradual development of trainings is foreseen from beginner-level (developed from Year 1**) to advanced levels (developed from Year 2, online and F2F BYODs). F2F BYODs are organized in WP14 as hackathons but are also the final step in learning advanced technical skills for creating and using FAIR data. Further, interdisciplinary F2F and on-line workshops on multiple research data flows will offer information and instructions to facilitate data network building and generate fair data ecosystems. This subtask contributes to the train-the-trainer aspect of BYODs, ensuring that participants become effective FAIR trainers themselves. **The expected numbers of trainees: up to 100 participants/year for online webinars available on the ERDERA website from Year 1; 20-30 participants of intermediate-level and BYOD online courses subsequently.** The F2F BYODs are expected to train up to 10 participants to the most advanced technical level. Conditions for train-the-trainer principle: In particular, the train-the-trainer principle is applicable to the BYODs. Courses, workshops and the generated material on data ethics and fair data ecosystem will be shared as Open Educational Resources.

T20.4. European Diploma on RD research (M1-M12) *TL: UCSC, IBG; Contributors: c4c-S, ISS, SU, UNIROMA1, ISCIII, ACU, UCD, RSU, VULSK, SFU.* T20.4. aligns with GO:1; SO:4,5; OO:3,4. This task aims to establish a higher education program culminating in an Academic Diploma with credits, through a collaborative effort involving a multi-stakeholder faculty of academic and non-academic partners experienced in training activities. The existing educational resources to train RD professionals are fragmented and uneven across EU/AC countries leading to inadequate knowledge. Targeting graduate-level students, the curriculum will cover RDs research innovation, also by leveraging previous initiatives like the EJP RD MOOCs. This initiative will pioneer the development of a standardized, graduate academic diploma program across the EU, establishing a professional profile for RD research experts. This qualification, currently absent on a global scale, will mark a significant advancement and empower the involvement and awareness of European universities in the field, beyond the existing commitment of individual instructors in RD training initiatives.

ST20.4.1. Establish a cross ERDERA expert consortium and setup of training modules *STL: SFU, UCD; Contributors: all task participants.*
Multilateral agreements will be made among academic and non-academic partners and connections with European University Alliances, to ensure policy alignment and improve geographical representation. The program set-up will be based on a minimum core-set of educational modules defining Entrustable Professional Activities (EPAs) for learners to demonstrate proficiency. The program design and set-up will be based on a minimum core-set of educational modules (10-12 foreseen) defining learning objectives, based on the Dublin Descriptors standards, along with Entrustable Professional Activities (EPAs) for learners to demonstrate proficiency, needed to implement the train-the-trainer principle. Principles of a program evaluation strategic plan will be developed at this stage. o
ST20.4.2. Pilot program launch (starts M13).
ST20.4.3. Optimization and scale-up of the program (starts M35).

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ST20.4.4. Running the first systematic EU diploma curriculum (starts M35).
ST20.4.5. Optimization and updating of study plan (starts M52).

ST20.4.6. Pursue future sustainability of the established curricula *STL: IBG, ISCIII. Contributors: all task participants.*
The task will consist of the analysis of components factors, and alternatives for ensuring the sustainability of the program, assessing its potential lifecycle. T20.4.6 will support the identification of potential stakeholders, including industrial and community partners, and other initiatives, in close collaboration with T20.4.1. Tools for visualizing the current disposition (visualization), for identifying risks and opportunities (SWOT) and for analysis of the potential business models (BM) and their configuration (Business Model Canvas (BMC) will be applied. This work will go through different processes:

- Current opportunities (as-is Business Model): identification of components, visualization, and SWOT.
- Alternative BM designs: Based on BMC results, applied to the pilot program launched (T20.4.2), searching and assessing different alternatives, including potential collaborations and stakeholders, risk management and costs calculation.
- Prioritization and milestones: Based on impact of the pilot program, a selection of BM and action plan will be put in place, considering the upgrades envisaged by T20.4.3.
- Implementation: execution of the model, applied to T20.4.4 and T20.4.5 work.

This will be done in close collaboration with the TLs of T1.5 (sustainability strategy), to ensure the complementary business and market vision. For the whole curriculum continuous evaluation, the RE-AIM (reach, effectiveness, adaptation, implementation, maintenance) method will be used. The goal of RE-AIM is that planners and evaluators pay more attention to essential program elements including external validity that can improve the sustainable adoption and implementation of effective, generalizable, evidence-based interventions.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**21**	**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Technology accelerator**					
Short name of participant & (No)	BIU (40)	CHARITE (44)	CIBER (125)	FHG (55)	CHI (45)	CNRS (124)	FDB* (155)
Person Months	0	17.70	5.98	20.60	6.50	6.62	6.00
Short name of participant & (No)	FSJD-CERCA (60)	FTELE (5)	IMAGINE (70)	INSERM_TARGET/ NANTES (1)	GNT (63)	INSERM_ART-ARNm (1)	UEF (113)
Person Months	7.70	3.56	6.5	1.4	17.90	2.46	8.94

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Short name of participant & (No)	KU Leuven (77)	OSR (89)	PEI (140)	UAB (110)	PLUS (141)	UKHD (13)	UC (28)
Person Months	12.29	14.31	12.08	6.64	5.10	0.97	19.08
Short name of participant & (No)	UKLFR (115)	AZ* (151)	VHIR (15)	HIPRA* (157)	LAB HIPRA* (158)	UCB* (167)	ROCHE* (165)
Person Months	2.62	8.80	4.38	3.57	1.92	7.20	4.80
Short name of participant & (No)	Miltenyi* (160)	Pfizer* (161)	REI* (163)	RJF* (164)			
Person Months	17.00	3.80	17.47	4.62			
Start month	M1		**End month**	M12			

**Associated partners providing in-kind contribution*

State of the art behind this WP

Traditional treatments for RDs are largely focused on treating symptoms. Given that approximately 80% of RDs are of genetic origin, advanced therapeutic medicinal products (ATMPs) have opened new opportunities for the treatment of RDs. ATMPs represent a ground-breaking approach to alter the genetic composition of cells to correct disease-causing mutations or to express proteins or RNA molecules that confer a therapeutic benefit. ATMPs offer thus the possibility of tackling the root causes of RDs and of finding cures. However, whilst the concept of gene therapy is a complex process comprised of multiple steps and components. This includes the right systems for getting nucleic acids into target cells, the right DNA regulatory elements that control the amount, location and duration of gene expression, and the efficient production of proteins with appropriate activity to alter cellular function in the desired manner. Development of effective and safe gene therapies requires not only novel technology, but innovative approaches to solve the technical challenges inherent to the research, development, and production processes. This includes effective and well understood translational science, robust and scalable manufacturing, well recognized and agreed standards, and critically a collaborative and networked ecosystem capable to move forward all these above-mentioned components together with the diverse technical challenges.

Recently, platform approaches and strategies have become a more efficient and a more common approach to address treatment or diagnostics development including CTs. The advantage of developing a “platform” technology is its capacity of adaptation or customization to specific needs based on a set of standardized tools or techniques. This allows to streamline the development process, reduce costs, and increase efficiency. To that end, in 2021, the National Institutes of Health (NIH) in the US, together with the U.S. Food and Drug Administration (FDA), as well as multiple pharmaceutical companies and non-profit organizations, launched the Bespoke Gene Therapy Consortium (BGTC). This consortium aims to establish platforms and standards to speed up the development and delivery of customized or “bespoke” gene therapies that could treat millions of people affected by RDs, including diseases too rare to be commercially viable. At the same time in Europe, initiatives like RESTORE5 or RARE-IMPACT6 contributed to a better understanding of the European setting for ATMP development and delivery. These initiatives demonstrated, on one hand, the exceptional potential of the European landscape that comprises multiple actors with high potential for creating disruptive ideas and technologies and, on the other hand, the overwhelming complexity of the delivery and treatment processes as part of the healthcare environment.

The Technology accelerator WP (WP21) is thus focused on streamlining the most promising gene transfer technologies (ATMPs) currently developed to fulfil the medical needs of genetically characterized RDs. By doing this, WP21 will create a unique network of expertise and excellence, ready to assist industrial and academic developers of ATMPs by enabling access to translatable, scalable, quality-controlled, and robust technologies, required to reduce the timeframe, the cost and accelerate clinical development.

Methodology

WP21 will be dedicated to accelerating key technology areas identified to be the most promising, and impactful for RDs. These include recombinant adenoviral vectors (AAVs) for gene therapy, therapeutic RNAs, novel and extracellular vesicles as vehicles, in vivo gene editing approaches, and strategies for monitoring therapy response (immune-mediated). For this, WP21 will focus on i) manufacturing processes based on state-of-the art technologies, ii) analytical methods and assays to better characterize these new medicinal products as well as to demonstrate their clinical utility and iii) technological tools to address evaluation of therapy response as well as immunogenicity issues related to *in vivo* administration of ATMPs.

To improve manufacturing, the approach will vary according to each type of ATMP. Today, recombinant AAV vectors are the most promising and efficient tool to achieve delivery of therapeutic DNA to various organs. However, long development time, expensive manufacturing processes and very high costs of goods, make these efficient therapies rarely accessible to many patients. WP21 will streamline cost-effective and harmonized AAV gene therapy development to make these vectors reach a higher number of patients across Europe. This will be achieved by bringing AAV expert centres that jointly will nurture standardization and quality control of AAV vectors. a
To address RNA-based therapeutic modalities, which are a rapidly growing field, with numerous CTs underway in the context of several diseases. WP21 has assembled renowned scientists working with RNAs in the context of several diseases (cancer, neurodegenerative and neuromuscular diseases) and spanning from design and manufacturing to *in vitro* and *in vivo* evaluation. RNA molecules can be used to target specific genes or pathways involved in disease processes and present a series of advantages including relatively low toxicity, reduced risk of accidental infection or opportunistic insertional mutagenesis. This is associated with a continuous breakthrough of delivery carriers, and potential of inducing both temporary or long-lasting effects. Therefore, different strategies will be tested for the design of more effective and stable RNA sequences. Small-scale manufacturing strategies of RNA *in vitro* transcription will also be assessed using *in vitro* DNA amplification from various DNA forms including optimizing methods for RNA purification.

Furthermore, WP21 will explore lipid (LNPs) which are considered as the current standard of mRNA formulations. Despite the success of mRNA vaccines against COVID-19, there are well known limitations for widespread use of mRNA for RDs. Extracellular vesicles (EVs) show promising capacity to deliver nucleic acids and reach tissues, or specific cells and intracellular targets that are not easily accessible to synthetic vectors, thereby opening new avenues for biotherapies. The goal of WP21 is to foster the development of novel types of nano(bio)particles including lipid (LNP), extracellular vesicles and biohybrids to deliver mRNA cargo more efficiently *in vivo*. To meet this challenge, partners gathering academic and private expertise will first gain a deep mechanistic understanding of the behaviour of current LNPs/EVs/ in terms of extracellular interactions and intracellular processing to enable rational design of novel mRNA/ formulations, including sustained release.

Finally, gene editing, which represents a new approach for precise manipulation of the human genome, will complete the technological focus of WP21. Furthermore, WP21 proposes to overcome the hurdles of gene delivery by using a variety of optimized gene editing (e.g., optimized Cas9 nucleases, base and prime editors) and delivery reagents (e.g., AAVs and NPs, as well as virus-like particles, VLPs) for efficient, targeted *in vivo* gene therapy.

This work will be complemented by a comprehensive safety assessment analysis including the evaluation of the potential (geno)toxicity and specificity. In addition, the increasing of efficiency of ATMP manufacturing processes will be accompanied by the development of innovative approaches to efficacy and quality controls. Generation of standard reference material will be a priority. Identity, potency, and safety tests will also be developed to comply with regulatory requirements. Novel methods to better characterize AAV vectors for clinical use will be developed, including evaluation of capsid heterogeneity, and precise measurement of empty or partially loaded capsids. These tests will be fully validated and the development of a miniaturized process for analytical assays will be considered. The quality control of mRNA will also be taken into consideration. Partners involved in the mRNA program will work on guidelines, requirements, standard reference materials and operating procedures to increase the robustness of the regulatory framework of RNA therapeutics. In addition, the WP21 program will also address a thorough evaluation of the various types of nanoparticles to be used for mRNA loading (i.e. LNPs EVs and nanoparticles). For each type of nanoparticles formulation, *in vitro* and *in vivo* evaluation of efficacy, pharmacokinetics, immunogenicity, and safety will be carefully defined in close connection with work dedicated to mRNA and to therapy response. Regarding gene edited cells, WP21 partners will screen optimized gene editing and delivery reagents (i.e., nanoparticles, EVs and VLPs) *in vitro* in human HSPCs. Next, the overall clinical efficacy of in vivo approaches will be assessed in relevant mouse models. After engraftment of human cells, appropriately vectorized gene editing tools will be injected in the bloodstream to target HSCs. In parallel, gene editing and delivery reagents (AAVs and nanoparticles) will be tested *in vitro* in CNS, liver, retina, and muscle cellular models. *In vitro* selected gene editing and delivery reagents will be tested in appropriate human organoid models, and/or humanized animal models to demonstrate efficient *in vivo* editing limited to the target organ and correction of the pathological phenotype. The safety of the different editing approaches will be assessed by a comprehensive analysis, of genomic off-target sites and of induced chromosomal rearrangements, in clinically relevant cell types. To uncover genome-wide off-target events, chromosomal rearrangements, and on-target aberrations in the *in vivo* edited tissues/organs, as well as persistence of off-target effects, analysis will be performed on genomic DNA and on cellular and plasma cell free DNA in longitudinal studies.

Therapy response represents a high unmet need to better characterize and monitor gene therapy approaches. Preformed or de novo unwanted innate (unspecific inflammation) and adaptive immune response (antigen-reactive T & B cells) to ATMPs have a major impact on safety (adverse effects by tissue injury and life-threatening side effects reported after Intravenous (IV) delivery of massive amounts of AAV viral particle) and efficacy (downregulation of therapeutic protein expression, removal of therapeutically modified cells), as well as on the feasibility of re-application of gene therapeutic tools (immunological pre-sensitization). Current diagnostic tools have several limitations (robustness, specificity, sensitivity, etc.). Developing advanced technology platforms, including devices and tests for preclinical characterization of gene therapy product candidates and further monitoring of therapy response in patients is essential to understand unwanted immune response. This will allow iterative refinement of gene therapeutic tools and targeted prevention/intervention in treated patients with RDs. In addition, improved analysis tools for assessment of (geno)toxicity to enhance safety and to predict efficacy and sustainability of innovative gene editing approaches is also needed. In this WP, experts in therapy response will work in connection with AAV, mRNA, nanoparticles and gene editing technological WPs to evaluate therapy response and bring a panel of improved and dedicated technologies and analytical tools that are critical for the development of safe and efficient ATMPs.

During the development of the AI-based system in ERDERA, the GAMP5[1] and Quality by Design[2] good practices will be implemented by addressing specific requirements all along the development

[1] Martin, K. C., & Perez, A. (2008). GAMP 5 quality risk management approach. *Pharmaceutical Engineering*, *28*(3), 24.

[2] Holm, P., Allesø, M., Bryder, M. C., & Holm, R. (2017). Q8 (R2) Pharmaceutical Development. ICH quality guidelines: an implementation guide, 535-577.

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cycle. Some of those requirements deal with the technical robustness of the AI technology. We have split up the tests into four categories:

Specifications of technical robustness:

- Performance of the tool will be demonstrated on a representative basis of the training dataset collected in real conditions. For each new modification, this performance test will be executed.
- Biases will be avoided by an appropriate data selection (training dataset) done in collaboration with biologists.
- A benefit/risk balance will be introduced to determine the acceptable risk related to the expected benefit.
- We will provide a confidence indicator of each prediction.

Social robustness:

- We shall have to demonstrate that the final product does not show any discrimination with regard to clinical parameters (sex, age, ethnic origin, etc.)
- We shall have to demonstrate the tool treat all patients fairly.

Reliability specifications

- We will introduce specifications and tests during the development to check that input requirements are correctly implemented.
- Quality by Design (ICH Q8(R2)) and GAMP5 involve risk analysis methods and tools (ICH Q9) to determine the risks associated with the use of the tool, implement means of risk control, reassess the residual risk and determine whether the latter is acceptable in view of the expected clinical benefit for the patient.
- If we need for information for the use of AI on personal data, GDPR will be validated in accordance with the obligation to provide information to the person concerned.
- Robust study (protocol) of AI performance with qualitative and quantitative metrics will be used.

Understanding the decision-making processes.

- We will provide a confidence indicator to give the researcher the ability to understand the result provided by the AI.
- We will work on the interpretability of AI to avoid a “black box” effect and control the entire development chain.

All those specifications are considered as Critical Safety Attributes that will be included in the pharmaceutical Quality by Design paradigm of development recommended by the FDA and EMA in the ICH Q8(R2) guidelines.

Objectives

In line with the aforementioned, the objectives of WP21 for Year 1 are:

- Definition of starting materials (plasmids, cell line, etc.) that can adequately support rAAV manufacture. In accordance, WP21 will start working on the establishment of a rAAV base manufacturing process in suspension cells using optimized plasmids/doggybone DNA; and in-house reference materials, as validation of assays for measurement of vector-related CQAs, and new assays to assess additional quality-related parameters or to replace existing analytical assays.
- Optimization of RNA sequence design to provide higher stability, long-lasting efficacy, and tissue/cell-specific expression. WP21 will also start working on the optimization of synthesis and purification processes of RNAs and on the development of an *in vitro* screening system to screen optimal RNA sequences based on RNA purity, immunogenicity, stability, and translation efficacy.
- Investigation of mechanisms underlying extracellular interactions and intracellular processing of LNPs/EVs to better understand LNPs/EVs uptake and trafficking, endosomal escape,

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delivery, macromolecular interactions, and biophysical processes in the cytosol of host cells and associated innate immune/inflammatory responses.

- *In vitro* selection of editing tools (i.e., combination of editing enzymes and gRNAs) and bespoke gene editing reagents to correct disease-causing mutations affecting human Hematopoietic Stem and Progenitor Cells (HSPCs), the central nervous system and the retina, and the liver and the muscle.
- Definition of test formats of different platforms used by the various partners of WP21 for in depth-assessment of immune reactivity and outline of a test strategy to get best comparability between labs. The first PoC studies using the different platforms to identify putative challenges in detection of rare events will be initiated. Round table meetings with leaders of task 21.1-21.4 will be also performed to evaluate and develop mitigation strategies to prevent/overcome unwanted immune responses. Cas9-specific Treg as model system will be explored and the best fitting Cas-specific T-cell receptor sequences will be selected.

Description of Programmed Activities

T21.1. Streamlining chemistry manufacturing and controls in AAV vector production (M1-M12) *TL: KU Leuven, UCB*, GNT. Contributors: VHIR, UC, UAB, INSERM_TARGET/NANTES, FHG, PEI, UKHD, REI*, Miltenyi*, FDB*, ROCHE**. T21.1. aligns with GO:2; SO:1,4,5; OO:1,2,5.
The overall goal of T21.1 is to enable cost-effective and harmonized AAV gene therapy development across Europe through standardization of manufacturing process and characterization of AAV vectors. These goals include:

- Agreeing on starting materials (plasmids, cell line, etc.) that adequately support rAAV manufacture;
- Agreeing and adapting a public background manufacturing process in suspension cells;
- Defining and validating fit-for-purpose manufacturing-related analytical assays;
- Developing novel technologies for analytical methods.

ST21.1.1. Establishment of a rAAV base manufacturing process in suspension cells *STL: GNT; Contributors: KU Leuven, UC, UAB, VHIR, INSERM_TARGET/NANTES, FHG, UCB*, PEI, FDB*, UKHD, REI, Miltenyi**
The base manufacturing process will be designed based on publicly available, state-of-the-art knowledge and methodologies identified after freedom-to-operate analysis. The process will be established on frequently used capsids e.g. AAV8 or AAV9. Variables that are required to adapt the process to other capsids will be identified (e.g. harvesting and downstream process development). Subsequently, **starting from Year 1**, T21.1.1 will define the characteristics of a non-proprietary, suspension producer cell line (e.g. growth conditions, average rAAV manufacture yield, etc.). If these cell lines are not accessible/appropriate, the use of a commercially available cell line will be considered. Next, T21.1.1 will assess and compare the characteristics of publicly available manufacturing plasmids across the different dimensions and align on best practice using publicly available information/methodologies as a starting point. This includes the sequence and constellation of the ITRs best suited to support efficient rAAV manufacturing; the elements of the plasmid backbone with respect to safety and optimal packaging (e.g. origin of replication, resistance gene, constitution of ITR flanking sequences etc.). For the helper plasmid, improvement will be gained through i) selection of promoters driving Rep/Cap expression which result in the highest yield and full/empty ratio; ii) defining the constitution and expression levels of Ad5 helper genes resulting in the highest yield and full/empty ratio.

Plasmids will later be tested in the suspension cell line selected in T21.1.1 at a scale of 25 ml using a publicly available production process for research grade production (after Year 1). Time permitted, transfer from plasmid format (3 best performing final plasmids) to doggybone DNA format will be evaluated and process development and scaling will be performed to assess if the doggybone platform yields a vector product of better quality at higher titres. A full agreement on requirements of base manufacturing process including acceptable starting materials and success criteria (productivity, recovery, contaminants) will be looked for with input from public and private partners. The next step

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will focus on adaptation of a 'public background' manufacturing process in (non-proprietary) suspension cells. This will be guided by the industrial partners. Finally, the robustness of the process will be tested by different partners on additional capsids/transgene cassettes at small scale during Y3. The process will be adapted to produce different vectors, including those needed for the gene editing studies described in T21.4 and the vectors that will be studied in T21.5.

ST21.1.2. Define and validate fit-for-purpose analytical assays for determining CQA-related rAAV characteristics and explore new technologies to develop more accurate analytical methods *STL: KU Leuven; Contributors: GNT, PEI, VHIR, UC, UAB, INSERM_ TARGET/NANTES, FHG, UCB*, REI, FDB, ROCHE**
Production of efficient and safe AAV vectors requires the set-up of several quality controls which rely on relevant analytical methods. **During Year 1,** T21.1.2 will first define a minimal set of analytical assays for purified vector to be used in preclinical development. A fit-for-purpose level of validation needed for different stages of preclinical development will be defined. The base manufacturing process defined in T21.1.1 requires assay(s) to determine vector yield in process. Academic and private partners will verify if this assay is fit for purpose. Where needed, the assay will be further optimized. Subsequently, T21.1.2 will start generating in-house standard reference material following the guidance of the Regulatory Support Group (WP18) and private partners. This will cover validation of the analytical assays identified above, using materials generated in T21.1.1, following the guidance of regulatory/private partners to assess selected CQA-related vector characteristics. The major CQAs include genome titre, capsid titre and full/empty capsid ratio. A focus on genome titre will be adopted, should all three CQAs not be possible. Later steps will focus on assay development and validation to assess additional quality-related parameters or to replace existing analytical assays.

T21.2: Advancing RNAs for therapeutics (M1-M12) *TL: UC, Pfizer*, FHG; Contributors: INSERM_ART-ARNm, CHARITE, UEF, PEI, FSJD-CERCA, GNT, RJF*, AZ*, Miltenyi*, HIPRA*, LAB HIPRA*, FDB**.T21.2. aligns with GO:2; SO:1,4,5; OO:1,2,5.
The activities planned in T21.2 are aimed at designing RNA constructs that are best suited for efficient production and incorporation into particles to deliver the relevant cargo to cells in vitro and in vivo. The main objectives of the T21.2 are to investigate novel approaches for:

- RNA design, to achieve higher RNA stability, translatability, cell-specificity, and lower immunogenicity.
- RNA manufacturing (RNA and DNA synthesis and purification), to allow more cost-efficient, safer, faster, and scalable manufacturing and downstream processes.
- Analytical characterization and screening of optimal RNA molecules.
- Proof of principle efficacy of RNA-based gene/base editing tools (Crispr/Cas9, Sleeping Beauty) in reporter cell lines.
- Large scale production of selected RNAs.

ST21.2.1. Design of RNA sequences (M1-M12) *STLs: CHARITE, INSERM_ART-ARNm; Contributors: UC, UEF, HIPRA**
Biologically active and effective RNAs depend on reliable design and preparation. **From Year 1,** T21.2 will start working on RNA sequence design using model RNAs such as GFP or luciferase as well as mRNA for gene editing tools such as Cas9 and transposase. T21.2 will focus on different regions of the RNA structures, including the 5' cap (development of cap analogues to prevent decapping at the 5' end), poly(A) tail (increase length), 5' and 3' untranslated regions (naturally occurring or synthetic), coding region (codon optimization using organ-specific codons or GC3-codons, for example, which increase transgene expression and stabilize RNAs due to a higher GC content, without affecting the amino acid sequence), and regulatory regions, which still need to be fully understood. Tissue/cell-specific expression (e.g., brain, muscle, liver, immune cells) will also be explored through the development of tissue-specific sequences.

ST21.2.2. RNA manufacturing *STL: UEF; Contributors: INSERM_ART-ARNm, CHARITE, Miltenyi*, FDB*, HIPRA**

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This task will be dedicated to the optimization of synthesis and purification processes of RNAs. **From Year 1**, T21.2.2 will focus on the optimization of RNA in vitro transcription (IVT) by engineering polymerases for high capping efficiency and high RNA yields and incorporation of chemically modified nucleotides (longer stability and lower immunogenicity). Different methods for RNA purification will also be explored (removal of free ribonucleotides, short RNA and DNA templates, and immunostimulatory contaminants).

ST21.2.3. Analytical characterization and screening of optimal RNA molecules *STL: FHG; Contributors: UC, INSERM_ART-ARNm, HIPRA*, GNT, FDB*.*
To evaluate RNA purity, immunogenicity, stability, and translation efficacy, T21.2.3 will develop an in vitro screening system for transgene expression determination and normalization to RNA content in cells, based on luminescent and/or fluorescent reporters. This system will be later used to reveal optimal RNA constructs regarding RNA sequence, codon usage, cap analogue, poly(A) tail, chemical modified nucleotides, and flanking UTR regions. Purity and stability studies of selected RNAs will also be conducted.

ST21.2.4. Proof of principle demonstration of efficacy and head-to-head comparison of selected RNA molecules in reporter cell line *STL: UC; Contributors: CHARITE, FSJD-CERCA, UEF, PEI, GNT, HIPRA*, FDB*.*
From Year 2, reporter cell lines will be used to assess and compare the efficacy of selected RNA sequences (e.g., delivery of mRNA for gene replacement or mRNA-based gene editing tools for stable gene therapy, namely CRISPR/Cas9 and Sleeping Beauty (SB) transposon technology).

ST21.2.5. Strategies for large scale production of selected RNAs (starts M36) STL*: FHG; Contributors: RJF*, Miltenyi*, HIPRA*, GNT*
The scale-up of RNA production presents unique challenges that will be addressed in this task in Year 3-Year 5. T21.2.5 will gather theoretical advice on the needs to scale towards clinical batches.
No activity is planned for Year 1.

ST21.2.6. Streamline of a robust regulatory framework for RNA therapeutics *STLs: Pfizer*, UC; Contributors: FHG, CHARITE, UEF, RJF*, AZ*, LAB HIPRA**
The rapid rise of mRNA therapeutics and advances in the field have not been accompanied by a robust regulatory framework. Partners from T21.2 will work in close collaboration with WP18 to have regulatory input and support around the tools and platforms being developed. T21.2.6 will work on the streamline of guidelines, requirements, standard reference materials and operating procedures for RNA therapeutics throughout the project.

T21.3. Advancing of novel types of mRNA nanoparticles including LNP, extracellular vesicles (EVs) and biohybrids (M1-M12) *TL: INSERM_ART-ARNm, Pfizer*, CNRS. Contributors: FHG, PEI, UC, CHARITE, CIBER, VHIR, PLUS, UEF, Miltenyi*, AZ*, RJF*, HIPRA*, LAB HIPRA*, FDB*, ROCHE**. T21.3. aligns with GO:2; SO:1,4; OO:1,2.
This task aims to advance the development of mRNA nanoparticles/EVs for gene editing of specific cells and organs as targets addressed in this project, i.e., hematopoietic stem cells, PBMC subsets, CNS, retina, liver, and muscle. This will be achieved in close collaboration with T21.2 for RNA design and production and T21.4 for gene editing evaluation in specific models. The specific objectives of T21.3 are to:

- Gain mechanistic understanding of current LNP/EVs extracellular interactions and intracellular processing enabling rational design of novel mRNA formulations, including sustained release.
- Develop computational tools to implement formulation design efficiency.
- Design standardized protocols for *in vitro* and *in vivo* evaluation of efficacy, pharmacokinetics, immunogenicity, and safety.
- Demonstrate of scalability of optimized mRNA nanoparticles formulations.

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- Compare and characterize PK and biodistribution of selected mRNA nanoparticles formulations from various routes of administration (i.v, i.m, i.p).
- Define regulatory quality control parameters of mRNA formulations in compliance with regulatory expectations and regulatory advice (de-risking approach to maximize the production of relevant mRNA formulations for clinical use).

ST21.3.1. Mechanistic understanding of current LNPs/EVs in terms of extracellular interactions and intracellular processing to enable rational design of novel mRNA formulations, including sustained release *STLs: INSERM_ART-ARNm, PEI; Contributors: VHIR, UC, CHARITE, Miltenyi*, CIBER, PLUS, CNRS, Pfizer*, AZ*, HIPRA*, FDB**
The goal is to gain a deep understanding on extra and intracellular barriers that mRNA particles formulations must overcome for an efficient mRNA translation. Benchmark of innovative formulations will be based on quantitative multimodal characterization and on quantitative assays of intracellular uptake of mRNA particles and mRNA delivery and translation. In collaboration with T21.2 partners, T21.3.1 will thus: i) Investigate the impacts of targeting and protein corona in the uptake on intracellular trafficking, endosomal escape of mRNA LNP/EV and mRNA translation efficiency (**Year 1**); ii) Mimic viral and/or extracellular vesicle (EV) uptake, release, and trafficking including lessons learnt from viral infection and EVs in terms of macromolecular interactions and biophysical process in the cytosol of host cells (Year 1 - Year 2); and iii) Characterize the innate immune response/inflammatory response following delivery of mRNA nanoparticles, especially in HSPC and PBMC subsets (Y2).

ST21.3.2. Development of tools to implement formulations efficiency *STLs: CNRS, RJF*; Contributors: INSERM_ART-ARNm, PEI, UEF, Pfizer*, HIPRA**
In-silico modelling and data-driven approaches emerged as indispensable methods for solving complex biological problems and their power has been particularly proven in projects related to ligand-target association, drug, and formulation designs. **Starting in Year 1,** T21.3.2 will apply and develop technologies for optimization and quality control (critical quality attributes) based on computational calculation to get a quantitative structure activity relationship (QSAR) of LNPs, EVs and biohybrids, using the multimodal data of T21.3.1. Two strategies will be pursued: (i) Quality by design methodologies (accelerated modular-orthogonal methodology for instance) to implement mRNA formulations and multimodal characterization of nanoparticles, EVs and biohybrids (ii) *In vitro* and *in vivo* translation models/predictions. Data-driven methods (using the data generated from partners before and during the project in T21.3.1-3) will be used to bring the systems and techniques towards technically robust, accurate and reproducible results in synthetic carrier design. Computational approaches will be used only to improve nucleic acids delivery in the specific tissue/cells of interest.

ST21.3.3 In vitro and in vivo evaluation of efficacy, immunogenicity, and safety of mRNA formulations *STL: CHARITE; Contributors: INSERM_ART-ARNm, CNRS, CIBER, UC, PEI, PLUS, Pfizer*, VHIR, HIPRA*, LAB HIPRA*, FDB**
From Y2, T21.3.3 will produce protocols on processes and methods-based on quality standards to evaluate pharmacokinetics and controlled release, biodistribution, efficacy, and immunogenicity and safety of mRNA formulations in vitro and in vivo. **No activity is planned for Year 1.**

ST21.3.4. Demonstration of scalability of targeted and optimized mRNA formulations made with synthetic nanoparticles and EVs *STL: FHG; Contributors: INSERM_ART-ARNm, CNRS, UC, CIBER, PLUS, RJF*, HIPRA*, LAB HIPRA*, FDB**
For clinical applications, it is crucial to select targeted and optimized RNA formulations that are amenable for large scale production in a cost-effective way. To reach this goal, from Y3, T21.3.4 will: (i) develop innovative loading processes of cargos for gene expression and editing purposes (ii) determine the most efficient targeting strategies for different types of formulations (iii) propose cost-effective methods for large-scale production of stable mRNA formulations. **No activity is planned for Year 1.**

ST21.3.5. Comparison and characterization of PK and biodistribution of mRNA formulations upon various routes of administration (i.v, i.m, i.p, i.p) *STL: CHARITE; Contributors: FHG, VIHR, Miltenyi*, CIBER, UC, PLUS, Pfizer*, RJF*, HIPRA*.*
After Y3, T21.3.5 will compare and characterize the stability and physicochemical interactions of RNA formulations without or with biomaterials and develop delivery/release devices to control pharmacokinetics and biodistribution. **No activity is planned for Year 1.**

ST21.3.6 Definition of regulatory quality control parameters of RNA formulations in compliance with regulatory expectations and regulatory advice *STLs: Pfizer*, UC; Contributors: CNRS, INSERM_ART-ARNm, FHG, VHIR, HIPRA**
Few studies are available to assist in the regulatory categorization of RNA-based products. Defining regulatory QC parameters is thus crucial. In this context, from Y2, in close collaboration with WP18, T21.3.6 will consider regulatory challenges with mRNA nanoparticles quality, starting material quality, release testing and characterization as well as regulatory challenges with EV and biohybrids encapsulating mRNA. **No activity is planned for Year 1.**

T21.4. Gene editing approaches towards therapy of RDs (M1-M12) *TL: OSR, Miltenyi*, IMAGINE. Contributors: UC, CIBER, GNT, UKLFR, BIU, UAB, FSJD-CERCA, FTELE, AZ*, Pfizer*, FDB*, ROCHE*.* T21.4. aligns with GO:2; SO:1; OO:1.
Gene editing has the potential to become a powerful new approach for the treatment of rare inherited diseases. The current gene editing tool of election is CRISPR-Cas9. This easy-to-program, RNA-guided system can be used to induce a DNA double-strand break (DSB) into a preselected site of the genome. DSB locally activates cell-intrinsic repair pathways, such as homology directed repair (HDR) and non-homologous end joining (NHEJ), which can be harnessed either to correct single point mutations and insert therapeutic cDNAs (using a co-delivered donor DNA temple) or to inactivate photogenic genes, respectively. Recent evolutions of the CRISPR-Cas9 system include base and prime editing. These tools can be used for single-base conversion or targeted insertion of short stretches of DNA. At variance with CRISPR-Cas9-mediated gene editing, base and prime editing require a single-stand DNA nick to operate, thus reducing the genotoxic risks associated with the induction of DSBs. Although promising, in vivo therapeutic application of gene editing is still limited by: (i) the paucity of gene delivery modalities compatible with effective, safe, and transient expression of the editing components; (ii) a full understanding of its genome-wide specificity profile, as editing may come with both on- and off-target consequences, including chromosomal aberrations and random integration of the donor DNA template. Overcoming these hurdles would allow to realize the full potential of gene editing.

The overarching goal of this task is to develop safe and effective in vivo gene editing strategies to treat paradigmatic rare inherited diseases affecting the blood, central nervous system, retina, liver, and muscle. Specific objectives are:

- To nominate combinations of bespoke editing reagents and delivery modalities in clinically relevant cell types from the blood, central nervous system, retina, liver, and muscle.
- To provide proof-of-principle of effective and safe correction of disease-causing mutations in vivo.

ST21.4.1. *In vitro* selection of effective gene editing strategies to target blood, neuronal, retinal, liver and muscle cells *STL: OSR; Contributors: IMAGINE, Miltenyi*, UC, CIBER, GNT, UKLFR, AZ*, FTELE*
This ST aims to identify effective and safe strategies for *in vitro* editing for RDs by comparison of editing strategies and delivery methods. **Activities will start from Year 1 and include:**

***In vitro* selection of bespoke gene editing reagents to correct disease-causing mutations in human Hematopoietic Stem and Progenitor Cells (HSPCs).** Here, T21.4 will tackle the following RDs: (i) Sickle Cell Disease (SCD), an hemoglobinopathy caused by a single point mutation in the beta-globin (*HBB*) gene, causing red blood cell deformation ("sickling") leading to anaemia, vaso-occlusive crises

and multi-organ damage; Fanconi Anemia (FA), a bone marrow failure syndrome characterized by chromosomal abnormalities and increased susceptibility to cancer and caused by mutations in the *FANC* genes that are involved in DNA repair; WHIM syndrome, an immunodeficiency caused by heterozygous Gain of Function (GoF) mutations in the *CXCR4* gene altering cell migration in response to SDF-1 (the ligand of CXCR4 receptor), calcium flux and causing neutrophil retention. As gene editing tools, T21.4.1 will exploit and compare the efficiencies of: (i) CRISPR-Cas9 and related orthologues, including recently developed engineered variants, such as SpOT-ON or HDR-CRISPR, that hijack the DNA repair pathways towards either non-homologous end joining (NHEJ, which leads to gene disruption) or homology-driven repair (HDR, which leads to gene correction and/or targeted transgene integration via a donor DNA template); (ii) base and prime editors, which allow to correct single point mutations and/or insert short stretches of exogenous DNA. For HDR-based approaches, as donor DNA template for gene correction and targeted integration, T21.4.1 will compare AAVs (from T21.1), Integrase Defective Lentiviral Vectors and single-stranded oligodeoxynucleotides (ssODN). Initial selection of editing tools (i.e., combination of editing enzymes and gRNAs) will be performed in cell lines (M1-M12). Validation experiments will be then conducted in HSPCs from either healthy donors and/or patients using the best-performing editing tools delivered either as mRNAs (in collaboration with T21.2) or as ribonucleoproteins (M13-M18). Subsequently, the following gene delivery modalities will be compared: (i) electroporation (an approach already available in the laboratories of the applicants); (ii) nanoparticles, EVs and biohybrids, which will be developed in T21.3; (iii) Viral Like Particles (VLPs) (M18-M48). Longitudinal analyses (e.g., NGS, ddPCR) of treated cells will be used to assess editing efficiencies and to identify the best-performing editing reagent for each disease. Phenotypic characterizations and functional assays (e.g., colony forming assay) will be used to assess treatment related toxicities. When possible, functional correction will be assessed by performing appropriate assays, for example erythroid differentiation and sickling assay for SCD, reversal of hypersensitivity to interstrand crosslinking agents (e.g., mitomycin C, MMC) for FA, and CXCR4 expression upon SDF-1 stimulation, migration assay and calcium flux for WHIM syndrome. All these assays are already established in the laboratories of the applicants. Overall, from these in vitro studies the best-performing editing reagents for each of the proposed diseases and effective gene delivery modality for HSPCs will be identified.

***In vitro* selection of bespoke gene editing reagents to correct disease-causing mutations affecting the central nervous system and the retina.** Here, T21.4.1 will tackle the following RDs: (i) Spinocerebellar ataxia type 3 (SCA3) by ablation of the expansion of the CAG triplet repeat in the *Ataxin 3* (*ATXN3*) gene or base-editing to induce exon-skipping (ii) Alexander disease (AXD) by either NHEJ-mediated inactivation or base editing-mediated gene correction of the *Glial Fibrillary Acidic Protein* (*GFAP*) gene; (iii) Amyotrophic Lateral Sclerosis (ALS) by allele-selective inactivation of the *Superoxide Dismutase 1* (*SOD1*) gene carrying the frequent GoF mutation c.11C>T; (iv) Retinitis Pigmentosa type 4 (RP4) by homology-independent targeted integration (HITI) of a corrective cDNA within the *Rhodopsin (RHO)* gene. Initial selection of editing tools (i.e., combination of editing enzymes and gRNAs) will be performed in cell lines (M1-M12), followed by validation in relevant human cell models, including (when available) immortalized cell lines and iPSC-derived cells from both healthy donors and patients (M13-M48). In these latter studies, different gene delivery modalities and donor DNA template formats will be compared. . Molecular analyses (e.g., on-target editing by NGS and gene expression) and phenotypic characterizations of treated cells will be used to assess editing efficiencies and treatment related toxicities, respectively. Functional correction will be assessed by the recovery of disease-specific pathological hallmarks (e.g., reduction in protein aggregates, improved survival of gene corrected cells). All these assays are already established in the laboratories of the applicants. Overall, from these studies the best-performing editing reagents for each of the proposed diseases and effective gene delivery modality for the indicated cell types is expected to be identified.

Selection of bespoke gene editing reagents to correct disease-causing mutations affecting the liver and the muscle. ST 21.4.1 will tackle the following RDs: (i) Progressive Familial Intra-hepatic Cholestasis type II (PFIC-2) by HDR-mediated insertion of a corrective cDNA within the disease

causing gene *ATP Binding Cassette Subfamily B Member 1* (*ABCB1*), which encodes bile salt export pump (BSEP); (ii) Duchenne Muscular Dystrophy (DMD) by CRISPR-Cas9 or base editing disruption of sequences inhibiting the expression of Utrophin, a protein that can compensate for dystrophin deficiency in DMD. Initial selection of editing tools (i.e., combination of editing enzymes and gRNAs) will be performed in cell lines (M1-M12), followed by validation in relevant human cell models, including (when available) immortalized cell lines, primary cells and iPSC-derived cells from both healthy donors and patients (M13-M48). In these latter studies, different gene delivery modalities and donor DNA template formats will be compared. Molecular analyses (e.g., on-target editing by NGS and gene expression) and phenotypic characterizations of treated cells will be used to assess editing efficiencies and treatment related toxicities, respectively. Functional correction will be assessed by the recovery of disease-specific pathological hallmarks (e.g., staining of the Dystrophin-Associated Protein Complex, for DMD). All these assays are already established in the laboratories of the applicants. Overall, from these in vitro studies the best-performing editing reagents for each of the proposed diseases and effective gene delivery modality for the indicated cell types is expected to be identified.

ST21.4.2. In vivo gene editing in model systems of the blood, CNS, muscle, retina, and liver *STL: IMAGINE; Contributors: OSR, UC, Miltenyi*, CIBER, GNT, FTELE, Pfizer**
This ST will combine the best-performing editing tools identified in Task 21.4.1 and will validate them in relevant in vitro 3D and in vivo mouse models of the selected diseases after Y2. **No activity is planned for Year 1.**

ST21.4.3. Unbiased, genome-wide specificity profiling of the best-performing gene editing platforms *STL: UKLFR; Contributors: BIU, OSR, FDB*, ROCHE**
This ST is focused on establishing a comprehensive safety assessment of the best-performing gene editing platforms developed under T21.4.1 and 2, thus creating standards and baseline data on the overall specificity and toxicity of the proposed genome editing processes. Individual tasks foreseen. **To be initiated in Year 2.**

ST 21.4.4. Detect the effects of gene editing platforms at the phenotypic level on different organs *STL: Miltenyi; Contributors: UC, FDB*, ROCHE**
This ST focuses on establishing comprehensive workflows to detect specificity and toxicity of the administered modalities in vivo at the phenotypic level. Activities will start in Y2.

T21.5. Assessment of therapy response and immunogenicity (M1-M12) *TL: CHARITE, Pfizer*; Contributors: CHI, Miltenyi*, ROCHE*, FSJD-CERCA, UAB, UC, OSR, INSERM_TARGET/NANTES, AZ*, UCB**. T21.5. aligns with GO:2; SO:1,4; OO:1,2.
The main objective of task 21.5 is to develop, qualify and validate innovative and complex platforms (tests + devices), used to characterize therapy response with a focus on unwanted immune reactions directed to vectors, RNA, lipid particles, gene editing tools, and therapeutic proteins and to develop mitigation strategies to overcome these unwanted effects. The specific objectives of T21.5 are:

- To challenge, develop and optimize advanced molecular and cellular test platforms, designed to investigate undesired innate and adaptive immune responses, in relevant in vitro and in vivo model systems.
- To use test platforms to measure the immune response directed to ATMPs developed within the T21.1-T21.4.
- To develop and implement strategies preventing/overcoming unwanted immune reactions directed to ATMPs platforms generated within T21.1-T21.4.
- To support the development of standardized tests for potency and (geno)toxicity.

ST21.5.1. Develop and optimize complex platforms for in depth-assessment of immune reactivity *STLs: CHARITE, Pfizer*; Contributors: CHI, Miltenyi*, ROCHE*, FSJD-CERCA, UAB, UC, OSR*
The ability of robust and meaningful analysis of therapy response is a key asset in optimizing therapeutic tools, patient selection, and prevention or management of adverse effects – in other words

contributes to de-risking and acceleration of the development of novel therapies. Therefore, T21.5.1 aims to determine whether there are tolerability/immunogenicity risks associated with ATMPs. This characterization allows to overcome several limitations regarding robustness, specificity, sensitivity, and information value of routinely used diagnostic tools (ELISpot, cytokine panel, whole blood assays etc.). As risks are identified, the development and optimization of complex platforms to measure therapy response to ATMPs become crucial. Task T21.5.1 will thus also target the development and optimization of advanced complex test platforms (devices + tests) for in depth characterization of immune response, **starting from Year 1**. These platforms will be tested on prototypes ATMPs delivered by T21.1-T21.4. These platforms will allow:

- **Deep analysis of innate and antigen-specific T-/B-cell immune response** to various ATMPs using molecular technologies such as, multi-omics single cell-technology (CITEseq, RNAseq, TCRseq, NGS), mass cytometry (Cytof), multiplex RT-PCR, multiligand assays, metabolic studies, and 3D lightsheet microscopy for understanding the impact of each immune cell repertoire to unwanted therapy response and designing test formats.
- **Development of complex and robust in vitro diagnostic platforms** supportive for the clinical development and implementation of ATMPs tools that are in the focus of T21.1-T21.4: Design of targeted molecular (RT-PCR) and proteomic (flow cytometry, or automated ELISA platform) or mixed (CITEseq/RNAseq) assays based on data from the deep analysis of innate and antigen-specific T-/B-cell immune response performed in T21.5.1.

Selection criteria for set-up of platforms will be high information value, sensitivity, robustness, with a high throughput, and feasibility. They should outperform currently used technologies to measure therapy response as Elispot, ligand quantification by ELISA, standard flowcytometry. These platforms will include the development of: (i) qualified targeted (with higher resolution) multiomics approach at single cell level to assess T-/B-cell and innate cell response (ii) qualified high-resolution flow cytometry assays to assess in vitro functionality of specifically triggered T-/B- and myeloid cell subsets, iii) assessment in vitro T cell functionality by targeted gene or protein expression panel as read-out following stimulation with specific reagents relevant to T21.1-21.4 Best performing and robust platform(s) will be selected and further developed with the aim to: (i) develop an in vitro/ex vivo transcriptomic or proteomics-based prototype analysing a set of targeted genes/proteins specific for T-cell response selected from T21.5.1 and assessed via the developed ATMP tools (T21.1-T21.4) (ii) develop a (semi)automatic bioinformatic pipeline to analyse multiomics single cell data for robust and fast assessment of immune cell response at high resolution based on data from T21.5.1 and proven with the developed ATMP tools.

ST21.5.2. Use in vivo and in vitro tissue model systems to verify the feasibility of test platforms developed *STL: INSERM_TARGET/NANTES; Contributors: CHARITE, Pfizer*, CHI, ROCHE*, FSJD-CERCA, UC, OSR, Miltenyi**
Peripheral blood samples and conventional in vitro 2D-cell cultures do not completely reflect intratissue immune processes, that are of major clinical impact. To allow high quality assessment of intratissue immune response, the test systems developed under T21.5.1 will be verified in more clinically relevant and complex *in vivo/in vitro* model systems and if necessary refined, taking into consideration age and gender aspects of the donors. Activities will start in Y2.

ST21.5.3. Qualified/validated selected test platforms to assess immune reactivity *STLs: CHI, Pfizer*; Contributors: ROCHE**
To bring tests from an exploratory level to decision-making tools, their qualification/validation according to regulatory requirements (FDA/EMA, GCLP, CE) is necessary. Complex test platforms will be assessed with inherent biologic variation, in accordance with regulatory guidelines for standardization. T21.5.3 will be initiated in Y3.

ST21.5.4. Evaluate and develop mitigation strategies to prevent/overcome unwanted immune response *STL: CHARITE; Contributors: T21.1-T21.4 partners, OSR, UAB, ROCHE*, Pfizer**

Commonly, current strategies to mitigate unwanted immune response directed to gene therapeutic tools are based on conventional steroid and sometimes calcineurin inhibitor treatment with limited efficacy and significant side effects. Moreover, assessment of preformed and *de novo* developing immune responsiveness lacks sensitivity and delivery of differential risk information making individual prediction of clinical impact difficult and therapeutic intervention mostly comes too late. The technologies developed under T21.5.1-3 and to be applied in CTs will deliver improved data for risk stratification regarding preformed and *de novo* immune reactivity. Identification of the unwanted immune response pathways (both preformed and *de novo* response) offer a better guide of immunomodulatory prophylaxis/therapy regime. Consequently, **T21.5 will follow two options, from Year 1:** (i) The design of gene therapeutic tools can be iteratively improved to minimize triggering of immune responses. This will be achieved with a feedback loop to improve iteratively, together with T21.1-T21.4, the design of gene therapeutic tools in order to achieve neglectable induction of unwanted immune response, (e.g. by CpG depleted or reduced transgene variants, altered Cas proteins codon optimization immune). (ii) Targeted immune regulatory interventions in patients receiving gene therapies can improve safety and efficacy profile of those therapies. Recent data show that regulatory T cells (Treg) can combat sufficiently undesired effector T cell response, opening a new option to reshape sustainably immune response. T21.5.4 will bring proof-of-principles of a novel approach based on generation of Cas-specific Treg by selective enrichment of antigen-reactive Treg or redirected specificity of polyclonal Treg (CAR, tgTCR) by gene editing and testing in preclinical model systems to combat Cas-specific preformed effector T/B response as first application case.

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**22**		**Start Date or Starting Event**		**M1: September 2024**	
Set of Activities Title	**Public-private collaboration accelerator**					
Short name of participant & (No)	EATRIS (22)	AFM (30)	FFRD (29)	ISCIII (72)	SRUMC (11)	EURORDIS (26)
Person Months	12	12	12	6	3	0
Start month	M1		**End month**		M12	

State of the art behind this WP

Translating scientific findings into socio-economic value in the biomedical domain is extremely challenging. High failure rates and long development times are hallmarks of the innovation process, with the average cost of each new medicine entering marketing authorization exceeding 2 billion USD. Early translation, identified as the development from first non-clinical proof of principle demonstrating the validity of a disease target to safe entry of a disease-modifying therapy into clinical development, is particularly difficult. Known as the 'Valley of Death,' early translation is nonetheless essential to conduct within academia and non-profit setting given the challenging market conditions for industrial development in RD. 'De-risking' projects is then necessary to build a dossier of knowledge about the target, disease, and intervention sufficiently strongly so that commercial and other stakeholders will invest in the costly clinical development pathway and implementation into the healthcare domain.

Challenges remain difficult and there is no over-arching framework to bring together all players. The creation of an accelerator framework brings to bear the significant public and private expertise in

disease biology and technology development, as well as the vast clinical expertise available in the CRNs and ERNs.

Methodology

De-risking involves several very important components, including a deep understanding of the disease phenotype and natural history, along with (ideally) a mechanistic understanding of the molecular basis of the disease. The former is essential in order to be able to gain meaningful clinical data on the performance of the novel intervention, while the latter provides a solid basis for developing non-clinical models and clinical biomarkers to evaluate the performance cost-effectively.

The goal of this accelerator programme through WP22 is working very closely with WP21 for best delivery technology selection – to develop and operate an integrated multinational and multi-stakeholder Research & Innovation ecosystem for RD focused on streamlining the process of advancing promising early-stage diagnostic or therapeutic intervention candidates into clinical development.

It will do so by creating and operating an innovation marketplace, supporting, and connecting promising RD projects with R&D experts, patients, and public and private investors, to enable further development with the aim of clinical implementation.

Objectives

The primary goal of the Accelerator is to create an integrated multinational and multi-stakeholder Research & Innovation ecosystem for RD (SO5) focused on streamlining the process of advancing promising early-stage diagnostic or therapeutic intervention candidates into clinical development (GO1 and GO2). The WP22 is dedicated to these two general objectives. Given the well-known challenge of moving from the technology push of (more academically-focused) scientific research into rigorous 'market pull' development of promising technologies and interventions – often known as the valley of death - this WP will assemble the know-how, facilities, patients, and investors necessary to successfully navigate translation. It will do so by creating and operate an innovation marketplace, supporting and connecting promising RD projects with R&D experts, patients, and public and private investors, to enable further development with the aim of clinical implementation.

Description of Programmed Activities

Activities for Year 1 will include the creation of workflows and legal documentation necessary to structurally identify, evaluate and select projects, the liaison with third party investors and innovation funders and the definition and readiness of the project selection process.

T22.1. Setting up the marketplace (M1-M12) *TL: ISCIII; Contributors: AFM, EATRIS, FFRD, SRUMC, EURORDIS.* T22.1. aligns with GO:2; SO:4,5; OO:3,5.
T22.1. is dedicated to esx. The task contributes to SO4, SO5 through OO3, OO5

ST22.1.1. Operational workflows *STL: ISCIII; Contributors: SRUMC, FFRD, AFM, EATRIS*
The following activities will take place in Year 1

- Establish of standard procedures for information sharing: Process workflows will be defined, and legal documentation created to facilitate information sharing in the accelerator and support the establishment of a strong legal framework. Feedback from stakeholders (industry, patients) will be integrated, and input from the Expertise Services Hub will be used as needed.
- The defined workflows will be collected in a set of Standard Operating Procedures (SOP) (Milestone MS22.1, accelerator workflows completed in M12) which will include legal documentation, with particular attention to confidentiality and conflict of interest statements. In order to present the accelerator mechanisms to potential investors, these SOPs will be summarised and made into a presentation deck.

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ST22.1.2. Liaison with prospective investors (public and private) *STL: FFRD; Contributors: ISCIII, AFM, EATRIS*

- From M6 FFRD will start liaising with prospective investors and bring them into the marketplace. Innovation support initiatives, (corporate) venture capital, SME and large pharma/biotech, philanthropic and charitable research funders, national public funders, and non-profit medicines access initiatives will be identified and approached. Those willing to participate will be onboarded by signing letters of intent that cover confidentiality, scope of engagement, selection criteria for projects, type of support, financing, intellectual property rights, exclusivity, and other features relevant to innovation support, like patient-centric research and patient involvement. Participating entities will form an accelerator community acting as follow-on support for RD projects. Experts from within this community will also be requested to join the pool of mentors in WP17 to be able to advise on exploitation and maximisation of results.
- Letters of intent and template project agreements will be publicized from existing resources such as the EATRIS Innovation Helpdesk and EJP RD IMT.

ST22.1.3. Project selection process *STL: AFM; Contributors: EATRIS, FFRD, EURORDIS*

- **Year 1** will be dedicated to defining the project selection process, criteria and usability to set up the outreach and project identification. This activity will be carried out in close collaboration with the WP3 JTC and the CRN workstream. Workflows for the exploitation of specific expertise will be designed in conjunction with WP17.

T22.2. Acceleration readiness (M1-M12) *TL: AFM; Contributors: EATRIS, FFRD, EURORDIS.* T22.2. aligns with GO:2; SO:1,4; OO:1,3,5.
This task's goals are to define a project selection process and criteria, ensure that ERDERA-funded projects are designed with exploitation in mind, projects scouted for their suitability for acceleration in a timely fashion, and to engage with other funding bodies to scout projects from other sources. **These activities will take place in Year 1.**

The project selection process will be defined in detail in close dialogue with the research funders and investors, based on criteria that ensure strong scientific rationale, clear unmet medical need, feasibility of route to market (manufacturing, scale-up, IP etc). Patient involvement in the selection process will be defined. Projects with a validated molecular target and suitable therapeutic modality for the disease context will be selected. AFM and FFRD will provide advisory services to the JTC funding secretariat and committee during definition of JTC calls to ensure that supported project results will be maximally robust and exploitable. Moreover, links with synergistic funding initiatives will be established so that high potential RD projects from these initiatives can be brought into the accelerator if there is capacity. This includes with ERA4Health, ERC, Horizon Europe Health Work programme and national funding initiatives. During JTC calls information sessions will be integrated in the call publication strategy, as well as monitoring process of JTC projects to ensure all applicants and principal investigators are fully aware of the requirements for further therapeutical development and the opportunities provided by the Acceleration Hub, Expertise Hub, and infrastructures. Annual meetings will be organized in liaison with JTC and monitoring WPs to identify JTC projects with potential for development into new intervention. Close collaboration with all WP22 partners will be sought for the selection of projects, with structural involvement of patient representatives in the selection process. Contributes to SO1, SO4, using OO1, OO3, OO5

T22.3. Asset profiling and development (starts M12) *TL: EATRIS; Contributors: AFM, FFRD, EURORDIS, ISCIII.* T22.3. aligns with GO:2; SO:1,4; OO:1,3, 5.
Selected projects will receive support defining an IPR, exploitation and patient access strategy, designing a critical path to proof of concept including stage gates and milestones, seeking funding for technical development. **No activity is planned for Year 1.**

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T22.4. Matchmaking and marketing (start M18) *TL: FFRD; Contributors: AFM, EATRIS.* T22.4. aligns with GO:2; SO:1, 4,5; OO:1,3,5.
Regular interactions with pharma and other potential funders will be scheduled to pitch projects and facilitate discussions and negotiations. **No activity is planned for Year 1.**

Additional deliverables *(additional to those included in part B of the proposal)*

None

Set of Activities Number	**23**		**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**NMG promotion and national alignment**						
Short name of participant & (No)	INSERM (1)	UNEW* (170)	CCUH (31)	UTARTU (9)	CCRI GmbH (42)	ISCIII (72)	VULSK (27)
Person Months	0	12	8	4	4	4	4
Short name of participant & (No)	ZonMw (7)	INSA (73)	MICYRN* (159)	INSERM_ U974 (1)	MUH (81)	TIF (107)	IBG (68)
Person Months	4	4	0	4	4	4	4
Short name of participant & (No)	HRB (67)	MoH SR (85)	RDG (86)	JSI (90)			
Person Months	4	4	3	0			
Start month	M1		**End month**		M12		

**Associated partners providing in-kind contribution*

State of the art behind this WP

The implementation of National Mirror Groups (NMGs) has been initiated under the EJP RD lifetime to facilitate the gathering of RD stakeholders at national level and form a link with activities and plans being delivered by large European consortia dedicated to RD. The added value of such groups has been identified through past projects and initiatives, in particular those highlighting the need to revive national commitments to RD. The first foresight study for RDs, Rare 2030, identified the fundamental need for 'A new EU policy framework for RD guaranteeing that RDs remain a public health priority through concerted European actions and guiding the implementation of long-term national plans and policies across all countries in Europe'. Rare 2030 also included several recommendations specifically around the need for greater connectivity and alignment of what happens at the national and European level, with enhanced opportunity for identifying and sharing good practices which are being employed

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in some places and could be translated to other national settings. The final project recommendations specifically mention the need to create more NMG, as a way to achieve this greater alignment. This is viewed as an important means of stimulating renewed national focus on maintaining dynamic and robust national plans for RD which has proved challenging for many European countries. NMGs also hold great potential to align national activities with the IRDiRC goals.

Developing and maintaining the functioning of the NMGs was a key component of the EJP RD T2.5. "Translation/impact of prioritization on national and EU strategies". Four EJP RD NMGs has been set up in Netherlands, Portugal, France, and the United Kingdom by the start of Year 2023. The establishment of new NMGs in the beneficiary countries has continued during the first half of 2023 and will remain a priority until the end of EJP RD lifetime in August 2024, so that as many EJPRD beneficiary countries as possible can benefit from a NMG (or a similar group) at the start of the ERDERA.

Methodology

Building NMG-ERDERA working relationships: Small group interactions will enable dedicated discussions between existing/future NMGs and the WP23 team, to better understand needs and expectations, which will be reflected in core outputs such as criteria and regular progress discussions.
Surveys and Questionnaires: A questionnaire will be co-developed with NMG input, to collect comparable semi-structured information (a mixture of quantitative and qualitative data) on national RD activities. A short separate survey will collect data related to KPIs agreed for the NMGs. This data will enable comparisons between countries, status quo assessments across countries under the ERDERA reach, as well as a longitudinal trend analysis.

Central to our methodology will be the organisation of a range of events, involving different actors with different goals. Three main levels are envisaged:

- **Annual meetings of each full NMG:** These will be overseen by the NMGs themselves, with WP23 input and support to agenda-setting (insofar as this is beneficial to ensure NMGs can meet the new agreed criteria – national needs and competences will be respected).
- **Annual meetings of NMG representatives:** These will be organised by this WP and will allow for a sharing of NMG experience and cross-fertilisation of expertise, in which achievements and good practices relevant to a range of countries will be presented. Needs and opportunities exchanged in these annual meetings will feed back into the following year's activity, to ensure a continuous cycle of reflection and improvement to task delivery.
- **Annual workshops focusing on key topics:** These will be co-creative interactive involving representatives of NMGs and ERDERA experts, intended to generate new knowledge and explore how to optimise synergies for greater alignment.
- **Delphi or mini Delphi methodology will be used to create valuable documents:** Best practice guidelines for NMG creation and promotion and recommendations for sustainability of NMGs.
- **Collaboration is needed with other ERDERA WPs:**
    - Other WPs on the Workstream on (Inter)national Capacity alignment: A specific collaboration work is expected and foreseen with the WP24 "Fostering engagement of underrepresented countries in ERDERA". WP24 leaders and contributors will use their knowledge of their RD community to help for the development of the NMGs within the different underrepresented countries. Besides, the NMGs will be an important tool that could help to understand the underrepresented countries' specific needs, foreseen in the WP24.
    - Workstream on Education and Training in RD Research
    - WP Communication
    - WP Monitoring of ERDERA activities

Objectives

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The main objective of this WP is to ensure the alignment of European and national RD research policies and activities by supporting, **during the Year 1**, the deployment and the operations of NMGs in all participating countries.

A NMG is a group created – or designated - in each country benefiting from the ERDERA to bring together the expertise and knowledge of the RD community of a specific country. The objectives of a RDs NMG are, on one hand, to identify national needs that should be discussed and addressed, if possible, within the framework of the ERDERA activities and, on the other hand, to promote national alignment with the European RD research strategy. In addition, the lessons learned, and good practices collected by each country are shared with the others. In this way, the activities of the ERDERA are more readily informed and shaped by heterogenous national needs and realities, whilst the tools, assets and approaches developed under the ERDERA (and EJP RD before it) are implemented more at national level, to advance RD research and innovation for all stakeholders. NMGs will help to align project activities with national policies and regulations. Additionally, NMGs can play a crucial role in advocating for necessary policy changes or improvements. By bringing together influential stakeholders and experts, NMGs can collectively identify policy gaps and advocate for reforms that would create a more favourable environment for the project's success. They can advocate for necessary policy changes to create an enabling environment for the project's success.

Specific objectives for the Year 1:

- Encourage and support the creation of NMGs in each country participating to the ERDERA and maintain them over time.
- Define and support activities under the responsibility of the NMGs.
- Develop networking and communication between the NMGs, fostering the opportunity for identification and sharing of good practices, feeding national needs and priorities into the ERDERA, and bridging the gap between national and European/international level activities.

This WP will, in particular, contributes to GO1 “Diagnosis established or enrolment in systematic research in average within 6 months after coming to medical attention”, the GO2 “1000 new therapies for RDs approved”, the GO3 “Better understanding of the impact of RDs on patients, families and society”, and will advance SO5 on the establishment of an “integrated multinational and multi-stakeholder R&I ecosystem for RDs” OO3 on “Coordination and alignment of European, (inter)national and regional research strategy and resources”, and OO5 on “Multi-stakeholder collaboration”.

Description of Programmed Activities

T23.1. Fostering creation of NMGs (M1-M12) *TL: INSERM_IT-GGB; Contributors: ISCIII, UNEW*, CCRI GmbH, UTARTU, IBG, CCUH, Inserm_U974, MUH, TIF, MICYRN*, VULSK, ZonMw, INSA, HRB, MoH SR, RDG, JSI, UO.* T23.1. aligns with GO:1-3, SO:5, OO:3.

ST23.1.1. Development of NMG models and guidelines

Setting up NMGs in each ERDERA beneficiary country first requires the development of specific guidelines and different models that can offer various alternatives to countries embarking on the process of developing NMGs. Indeed, the experience of the EJP RD has shown us that each beneficiary country has its own specificities, both in terms of structure (centralized organization/federal organization for example), and in terms of national organization and the state of the art in RD research. Taking these differences into account is essential as each NMG has represent the RD community in its own country. **In Year 1**, the first task of the TL and the partners will be to develop, in the first four months of the project, several models of NMGs, based on the study of the national groups set up during the lifetime of EJP RD. These different models, which will differ in several aspects (size of the NMG, spectrum of stakeholders to be involved, organization scheme to be adopted, etc.), will be used on the NMGs development process on the T23.1.2. Several criteria are foreseen:

- NMGs must bring together the national representatives of all relevant RD stakeholders of a country (as described in ST23.1.2).

- Each NMG must choose a leader/contact point among the representatives' organisations that constitutes the group in order to ensure the contact with WP23 leaders, with others NMGs and to ensure the smooth implementation of the activities foreseen (as described in T23.2.). This national contact point must be a beneficiary organisation of the ERDERA.
- NMGs must respect a wide geographical representation of their country.

ST23.1.2. Developing & maintaining NMGs through a national multi-stakeholder engagement
The objective of this task is to have an NMG established in each beneficiary country of the ERDERA by the middle of Year 2 of the project (M18). **During Year 1**, the NMGs will be set up and supported to organize coordinated interaction between the Partnership and national and regional stakeholders. They will catalyse the transfer of good practices to the national and regional level. As NMGs will serve as intermediates between the Partnership and national and regional stakeholders in the field of RDs, they need to bring together the national representatives of the ERDERA and other relevant RD stakeholders from their country: Research institutes, National Alliances, Patient organisations, national/local authorities, funding agencies, hospitals, health care partners (affiliated or not with the ERNs) members of the ERDERA Policy Board & Governing Board. NMGs models and guidelines developed on the T23.1.1. will be shared with the national stakeholders involved in the NMG development process, proposing several configurations to ensure optimum inclusion of multiple stakeholders within a functional group. The development of these NMGs will also consider the presence (or absence) of existing national RD groups in order not to duplicate efforts and to collaborate with experienced local and national actors.

Rare Diseases NMGs are expected to last over time and operate efficiently over the long term, having important responsibilities, described in task 23.2. Each NMG will be piloted by a manager who can ensure the proper functioning of the NMG and who can be the intermediary with the coordination team, the WP, and TLs and with the managers of the other NMGs, to ensure that the objectives set for each NMG can be/are achieved. **The objective of this task for the Year 1** of the ERDERA (M1-M12) is to develop a NMG in at least 75% of ERDERA beneficiary countries.

It is expected that the following countries will have an operational NMG built by the start of the ERDERA: Austria, Belgium, Canada, Cyprus, Czech Republic, Estonia, France, Ireland, Latvia, Lithuania, The Netherlands, Portugal, Slovakia, Spain, Türkiye, and United Kingdom.

The development of NMGs in the following countries is scheduled to take place in the Year 1. These countries should therefore have an operational NMG by September 2025: Australia, Belgium, Bulgaria, Denmark, Finland, Georgia, Germany, Greece, Hungary, Iceland, Israel, Italy, Luxembourg, Malta, Morocco, New Zealand, Norway, Poland, Romania, Serbia, Slovenia, Sweden, Switzerland.

T23.2. Deployment and operation of NMGs (M1-M12) *TL: UNEW*; Contributor: INSERM_IT-GGB; ISCIII; CCRI GmbH, UTARTU, IBG, CCUH, INSERM_U974, MUH, TIF, MICYRN*, VULSK, ZonMw, INSA, HRB, MoH SR, RDG, JSI, UO.* T23.2. aligns with GO:1-3; SO:4,5; OO:3,4.
This task will contribute to the GO1 “Diagnosis established or enrolment in systematic research in average within 6 months after coming to medical attention”, the GO2 “1000 new therapies for RDs approved”, the GO3 “Better understanding of the impact of RDs on patients, families and society”, to the SO4 “Increased capacity and skills of RD stakeholders to optimize research to healthcare continuum”, the Specific Objective SO5 “Integrated multinational and multi-stakeholder Research & Innovation ecosystem for Rare Diseases”, the Operational Objective OO3 “Coordination and alignment of European, (inter)national and regional research strategies and resources" and the Operational Objective OO4 “Training and education (of RD stakeholders).

ST23.2.1. NMG Responsibilities
As new NMGs are created, linked to ERDERA beneficiaries, they will be required to fulfil a number of core activities each year in order to ensure the best collaboration possible with ERDERA. These will be clustered around three categories:

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- Activating and operationalising a national-level community engaged in RD research (for instance through regular communications and meetings): The NMGs should contribute to the support of alignment and integration of national capacities into the Partnership. NMGs should also encourage the development and the promotion of National RDs plans/strategies.
- Feeding national needs and realities into ERDERA meetings and activities, to optimise the relevance of the ERDERA outputs;
- Taking active steps to align national-level research resources, infrastructures and approaches to those being developed and disseminated under the ERDERA; and providing data on national activity and NMG progress.

The expected responsibilities of each NMGs can be detailed as the following:

1. To create and write a three-year plan based on current needs and interests of particular country in which fields NMG has to work more actively, where to pay more attention (for example, encourage colleagues for more active usage of Orpha codes, embolden to create new patient organizations for certain disorders): this plan must be updated every year. This plan is expected to consider the national-level community engaged in the ERDERA, as do the national stakeholders that are not part of it.
2. Every year each NMG must complete surveys organized by WP leaders as well as self-evaluation form, naming all activities performed during the past year.
3. Each NMG should organize, regarding of the specific national needs, at least once per year face to face local meeting, including educational session.
4. Representative from each NMG (likely the contact point described in task 23.1.2) should take part in the National Alignment Board annual meeting as indicated in T23.3.1
5. NMGs members must participate in workshop described in T23.3.2 and later are responsible for knowledge dissemination among members of NMGs.
6. NMG must be actively involved in promotion of National RDs plan as far as it is possible. Preferably national policy makers should be part of NMGs. In case it cannot happen, NMGs should interact with government and in the frame of their possibilities facilitate plan writing and execution.
7. At least one representative from each NMG must be interactive and communicative with other NMGs sharing their local experience and gaining knowledge from others using platform described in T23.3.2.
8. Local NMG representatives should be aware of ERDERA activities and be capable to disseminate information among group members which are less actively involved for e.g. policy makers. And on the other hand board member must be capable to present specific local capabilities which may serve in the interests of partnership which main goal is to improve care of RD patients.

During Year 1, the already developed NMGs will have to endorse these responsibilities.

ST23.2.2. Country-Specific bidirectional Engagement

Based upon the criteria guidance agreed in task 1, regular internal communication meetings (online meetings every 3 months) will be organised within each NMG leadership team, to support the alignment with the ERDERA activities. These will fit under a number of headings (e.g. national RD research programmes, clinical research capacities, large data infrastructures relating to registries and biobanks, diagnostics structures/databases, socially oriented research, etc.). These meetings will, where appropriate, involve representatives of other ERDERA WPs, to unite topic experts from the ERDERA with NMG leads and offer advice or support with aligning national systems or structures more with the tools and approaches being deployed by ERDERA. These calls will also be opportunities for the ERDERA task Leads to learn more about national needs and priorities and identify successful and/or innovative approaches to addressing particular RD research challenges. They will share the results of any national-level mapping of networks or hubs which could bring value to the ERDERA but are not yet included in ERNs – and, in the case of those from countries not eligible for formal ERN

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engagement, this intelligence-gathering could support collaboration of researchers from outside of the EU/EEA, complimenting efforts already underway to enable this. An important added value of the NMGs is their potential to contribute to the maintenance of robust, in-date national plans or strategies for RD: in many countries, following the expiry of a time-bound plan, there is no prompt evaluation of the impact of the original policies, and no follow-up plan is adopted. The engagement of the ERDERA with NMGs through this task will therefore seek to encourage and embed good practices in this regard, as far as this can be influenced by the NMGs. **Starting from Year 1,** regular meetings, taking place every three months, will be set-up within the leadership team of each NMG to support the alignment of national and RD P activities. Particularly in **Year 1** of the project, these meetings will be an opportunity for task leads to gain information about each NMG's national activities. Representatives from other WPs will be invited to attend these meetings, where appropriate, to help in shaping the three-year plans whilst offering advice and support on aligning with different ERDERA activities, resources, and tools. It is important to do this early in the project to ensure resources being developed within the ERDERA meet the needs of the NMGs.

ST23.2.3. Country Data Collection
The emergence of a greater number of NMGs and prospective NMGs offers an excellent opportunity to collect rich data on national activities of relevance to RD. This will help to understand the national status quo but also allow for comparisons between countries. A questionnaire will be redesigned (using the old Resource on the State of the Art of RD Activities in Europe) as a guide, which captures not only relevant national activity but also international collaborations. (This could be a means of continuing some of the work conducted under WP2 of the EJP RD, and would also be a new home for the 'State of the Art Resource' (which has not had a home since Rare 2030). Associated outputs will be a dedicated annual report for each country participating to the ERDERA (in the case of those with NMGs, UNEW would ask leads to provide this data – ensuring a multistakeholder composition: for those without, UNEW would use existing contacts from the 'State of the Art Resource' and EJP RD WP2 team to request data nonetheless, for completeness). Synergies with Polaris platform will be ensured to avoid any duplication of data collection. Data collected by the NMGs about the state of each country in the field of RDs must be compliant with the KPIs of the ERDERA: it is expected from the NMGs leaders to provide information regarding the undiagnosed programs, the policy changes or initiatives at local and national levels aiming at addressing the impact of RDs on patient, families, and society.

In Year 1, those questionnaires will be developed by the TLs. Beginning in M6 of the project, task leads and beneficiaries will design and pilot a questionnaire, using the questionnaire utilized for the 'Resource on the State of the Art of RD Activities in Europe' as a guide. The purpose of this survey will be to capture relevant national activity, as well as international collaborations, to support more effective NMG operations and support inter-NMG activities for task 23.3 When developing the survey, task leads will look at synergies with the Polaris platform to avoid duplication. A first round of collecting national data reports will be organised by M12.

ST23.2.4. Trainings activities through the 'Train the trainer model'
This sub-task is foreseen thanks to a collaboration work with the ERDERA Workstream 'Education & training activities' and is planned to start during Year 2. A series of training activities for national stakeholders is planned as part of this subtask topics of the training activities will be drawn up in collaboration with the various National Mirror Groups to best meet their needs.

T23.3. Animation of NMGs synergies (M6-M12) *TL: UNEW*, CCUH; Contributors: INSERM_IT-GGB, UTARTU, CCRI GmbH, ISCIII, VULSK, ZonMw, INSA, MICYRN*, INSERM_U974, MUH, TIF, IBG, HRB, MoH SR, RDG, JSI, UO.* T23.3. aligns with GO:1-3; SO:5; OO:3,5.

ST23.3.1. National Alignment Board during the annual International NMG meeting
Representatives of NMGs will be key participants to the annual meeting of the National Alignment Board (NAB), held likely back-to-back with the annual General Assembly. This International NMG

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meeting will also involve representatives (ideally from Competent National Authorities or key Research funding institutions, with some oversight of RD research activity in their country) to attend, whilst we await 'formal' creation of NMGs. As described in the 'Governance' section, the NAB will be composed of Representatives of each National Mirror Groups and Representatives of the European Commission Directorates: DG Research & Innovation, DG Joint Research Centre (JRC), DG SANTE, DG CNECT. A chair will be selected by and within the member of the NAB. Its role will be to ensure that national/EU activities, strategies and needs are considered when taking decisions at the ERDERA level and when designing the AWPs. In the Annual meeting of the National Alignment Board, NMG leads will share progress on the creation and operations of NMGs, and steps taken to align national and ERDERA level activity. This meeting will seek to highlight success stories (where NMGs have been able to take concrete steps to either shape development of ERDERA tasks or embed ERDERA learnings or tools into their national level, in some way) and to share good practices. In so doing, WP23 coordination team will take care to consider examples and successes replicable for certain types of countries e.g. showcase solutions being advanced or explored by small countries, by large countries, cross-country collaborations (e.g. where countries are working on something as a region). WP23 coordination team will work closely with WP24 on Underrepresented Countries here, to ensure the particular needs and realities of these nations are represented and solutions can be found for the additional challenges they might face. During first three annual meetings the best practice guidelines of creation and promotion of NMGs will be developed, as during partnership NMGs will be created in ERDERA country beneficiaries. Sustainability is as important as creation of NMGs during annual meetings starting from year for recommendations for sustainability will be developed, it will include - identification of sustainable elements for NMGs and actions needed to successful continuation of active action after end of partnership.

The 1st NMG International meeting will took place during Year 1. In Year 1 of the ERDERA, participants involved in ST23.3.1 will arrange the first NAB meeting. The purpose of this meeting is to share progress on the creation and operations of NMGs, showcase alignment of ERDERA and national activities, highlight success stories and share good practices. The NAB meeting will likely be held back-to-back with the general assembly, most probably happening on September or October: collaboration with the coordination team will be required to organize this meeting. Representatives of NMGs, as identified in T23.1., will form part of the NAB, and will be invited to attend.

Particularly within Year 1 of the project, whilst NMGs are being established, two representatives from each NMG, (ideally from Competent National Authorities or key Research funding institutions, with some oversight of RD research activity in their country) will be identified and invited to attend the first NMG meeting.

Collaboration with WP24 on underrepresented countries will be needed to ensure the particular needs and realities of these nations are represented. In the first NAB meeting, as well as the following two meetings, there will be a focus on development of best practice guidelines of creation and promotion of NMGs. Best practice guidelines for creation and promotion of NMGs will begin to be developed within the first meeting.

ST23.3.2. Fostering interaction between NMGs, to enhance cross-country collaboration
This task will foster stronger interactions between NMGs –and thus countries- at the 'topic' level (whereas 23.3.1 is more about sharing learnings and progress in developing and mobilising NMGs broadly, and sharing their views on the ERDERA direction, how the ERDERA can best support them, etc). WP23 leaders will organise workshops dedicated to topics of key importance for the advancement and optimisation of RD research, which will be aimed at representatives of NMGs and will also involve experts leading work related to these topics from within the ERDERA. These will foreseeably include subjects such as creation/adaptation/federation of national registries for RD, linking national diagnostics structures with ERDERA resources, optimising CT planning and delivery, national drug reimbursement programs, NBS etc. The goal will be to make NMGs aware of the latest developments and assets provided by the RD (allowing the NMG representatives to influence future development of

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these, in view of their needs and own national successes/challenges here) and support countries in making their own approaches and infrastructures and systems more 'ERDERA-compatible'. These workshops will largely be about generating new knowledge and will therefore be a key means of fostering tangible alignment between national and European activity, as opposed to imparting established training. In planning and delivering each workshop, the needs and voices of different types of countries will be considered, avoiding a 'one-size-fits-all' approach (close collaboration will be ensured with WP24.) One face-to-face workshop per year will be organised, with the option to hold an additional virtual workshop each year. The focus of these will be agreed each year by the NMG leads attending the National Alignment Board. Within ST23.3.2, it is foreseen that in each year of the project, a workshop will be developed on topics of key importance for the advancement and optimization of RD research.

In Year 1, most probably in May, the first face-to-face workshop will be developed and organized by sub-task leads. The organization will include identifying a suitable venue for the workshop and inviting attendees, who will be NMG representatives. The topic of the workshop will be agreed by existing NMG leads via choosing the best probable topic offered in survey by WP leads. Close collaboration with WP24 and other WPs will be needed to develop the agenda for the workshop, to ensure the raising of awareness of the latest developments and assets provided by the ERDERA. In addition to the in-person workshops, participants in this sub-task will also explore the potential of developing a further online workshop.

To achieve best possible results, dynamics, and sustainability of NMGs, but at the same time to maintain formality and to avoid lack of information and support in between different NMGs, regular networking is needed. Day-to-day networking on everyday practice will be organized through multifunctional platforms where information can be stored and shared. Usage of such a platform will allow collaboration between different NMGs on a weekly or even daily basis. This platform will be open and accessible to the WPs leaders of the ERDERA and will be at the centre of exchanges between all these stakeholders: the representatives of the NMGs will be able to call on the WPs leaders to strengthen the alignment of their countries on specific topics, and the WPs leaders will have easy access to the data provided by the countries and to their national expertise. This approach would also be important to exchange experience and knowledge of some subgroups of NMGs as for example from small countries or regional specificities.

Using available ERDERA platforms, **this platform and communication channels will be developed during the Year 1** to allow networking between NMGs and the consortium and the sharing and storing of information between NMGs on a daily and weekly basis. This will help to allow the sharing of best practices.

ST23.3.3. Sharing achievements of NMGs.
During the first three years of partnership using the outputs of T23.2.3, an overview report will be developed every year, arranged by topic (e.g. showcasing the situation and trends around live national plans for RD, national registries for RD, etc) **During Year 1,** three annual reports will be produced, to summarise key achievements across NMGs, illustrating development of NMGs, providing examples of key activities and successes, and generally publicising the data collected in Task 23.2.4 as above. During Year four to seven based on collected information and achievements at two peer-reviewed publications in open access journals will be published during project with a purpose to reach out more health care specialists, for example GPs, clinical specialists, and scientists from other fields. As well as four overview reports will be developed, and four annual reports will be published on website regarding ongoing activities and collaborations of NMGs. Suitable communication channels will be explored, in collaboration with WP2, to publicise national plans externally. **The first annual overview report will be developed in Year 1**, using the outputs of T23.2 and T23.3, to highlight the key achievements across NMGs, development of NMGs, provide examples of key activities and successes, and publicise data collected in T23.2.4.

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Additional deliverables *(additional to those included in part B of the proposal)*
None

Set of Activities Number	**24**		**Start Date or Starting Event**		**M1: September 2024**		
Set of Activities Title	**Fostering engagement of underrepresented countries in ERDERA**						
Short name of participant & (No)	AICIB (32)	REUH (93)	FFRD (29)	RDB (131)	RIF (94)	ZonMw (7)	EUROR DIS (26)
Person Months	9.87	6.59	2.14	0.71	2.58	2.58	6.43
Short name of participant & (No)	RSU (96)	TUBITAK (108)	IBG (68)	IMGGE (33)	CVBF (50)	HRB (67)	VULSK (27)
Person Months	0.71	2.58	5.3	8.4	3.3	2.58	9.2
Short name of participant & (No)	CAU (123)	UCD (111)	GERAD (64)				
Person Months	2.14	3.14	3.14				
Start month	M1		**End month**		M12		

State of the art behind this WP

In an increasingly interconnected global Research and Innovation (R&I) landscape, it is of utmost importance to perceive that Underrepresented Countries (UCs) often face unique challenges when it comes to participation and contribution on the European and International stage. Despite several institutional efforts to increase inclusiveness, significant discrepancies between countries' performances in what respects to R&I are still highlighted in official reports, as the recent Survey Report from ERA-LEARN Inclusiveness in European R&I Partnership Programme, which points out the "lack of a systematic approach towards enhancing participation of Widening Countries in the (EU) Programmes"[19]. RD field is not an exception, although efforts to increase UCs participation were undertaken in EJP RD. However, these measures were mainly applied in JTCs (and capacity building activities), thus limiting its reach, and not solving the problem.

ERDERA intends to have an increased and proactive role in facilitating closing the gap between RDs R&I high and low performing countries. This is most pertinent if we consider that 20 out of 29 ERDERA participating countries are UCs. Thus, this WP, in close articulation with the other WPs of the Partnership, is purposely designed to address these inequalities and unlock the potential present within UCs. The role of the so-called ERDERA high performing countries in this WP is highly relevant, not only for knowledge exchange and benchmarking exercises but also as facilitators of inclusiveness.

Methodology

WP24 is fully aligned with the Strategic Research and Innovation Agenda (SRIA) of ERDERA, in particular with the GO3: Better Understanding of the Impact of RD on Patients, Families and Society; the SO3: All activities empower, as equal partners, people living with RD; the SO4: Increased capacity and skills of RD stakeholders to optimise research to healthcare continuum; the SO5: Integrated multinational and multi-stakeholder R&I ecosystem for RD; and the OO3: Coordination and alignment of European, (inter)national and regional research strategies and resources.

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The methodology underlying the Tasks (involving various partners/contributors) comprise a combination of mapping exercises, assessments, knowledge exchange, collaboration with relevant entities, benchmarking, and the development of guidelines and programmes. The Tasks aim to identify specific needs and expectations, assess conditions and barriers, establish synergies, undertake advocacy and awareness-raising actions, identify measures for increasing participation, analyse and adapt existing measures and guidelines, and explore additional financial support. It will resort to outputs from previous initiatives, surveys, and relevant findings to inform decision-making and proposal development. A collaborative and multidisciplinary approach will be implemented (involving the full spectrum of partners: universities, hospitals, research organizations, patient organizations, and foundations) to address the challenges and gaps in RD R&I.

Overall, it will be emphasised the processes of data gathering, analysis, collaboration, knowledge sharing, and the development of practical guidelines and programmes to promote capacity development, advocate for underrepresented countries, improve participation, and facilitate mobility opportunities.

Close collaboration is envisaged with other ERDERA workstreams and WPs:

- Other WPs on the Workstream on (Inter)national Capacity Alignment (e.g. WP23: joint efforts on the unmet needs of UCs through NMGs activities), Workstreams: RD Funding, Education and Training in RD Research.
- WP1 T1.3. Monitoring of ERDERA activities.

Objectives

The objectives of the WP24 for the Year 1 are:

- Promote transversal, coordinated efforts in mapping capabilities and assets, and capacity development.
- Build synergies with JARDIN, EURORDIS, HNN3.0 (Health NCPs), NFP4EU (Health NFPs), and the NCP_WIDERA.NET
- Foster collaboration between UCs and Research & Innovation (R&I) high performing countries at European level.
- Preliminary measures to boost inclusion of UCs in ERDERA funded projects.

Description of Programmed Activities

T24.1. Promoting capacity development actions (M1-M12) *TL: VULSK, REUH; Contributors: EURORDIS, IBG, CVBF, GERAD, UCD.* T24.1. aligns with GO:3, SO:4-5.
In Year 1 of ERDERA, VULSK and REUH will conduct a mapping exercise to identify the specific needs and expectations, perceived by UCs, limiting their full integration in RD R&I. In particular, the conditions for their full integration across all ERDERA activities (JTCs, CRNs, Acceleration Hub, Data Services Hub, Support Services, etc.) will be assessed, with attention to barriers to participation in CTs. In addition, knowledge exchange and mutual learning exercises will be carried out between UCs (research actors, patient organisations) to learn from each other and promote the implementation of activities at the national level to foster participation in ERDERA. This should complement efforts to coordinate the NMG representatives. Focused engagement with high performing countries in R&I will be also carried out to integrate their learnings and expertise.

ST24.1.1. Mapping to determine needs and expectations of UCs aligned with ERDERA workstreams *STL: REUH; Contributors: VULSK, EURORDIS, IBG, UCD, GERAD.*
Within this ST, a mapping exercise will be conducted, to identify the most pressing needs and expectations of under-represented countries in ERDERA, including information on current barriers to participation.

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ST24.1.2. Knowledge exchange, mutual learning exercises and benchmarking with RD high performers (UC and high-performing countries) *STL: VULSK; Contributors: REUH, EURORDIS, IBG, UCD, GERAD.*
Within this ST, interaction activities will be organized and conducted between UCs and high performing countries, to strengthen UCs' capabilities and promote their active participation in ERDERA.

T24.2. Undertaking advocacy and awareness efforts to UCs added value (M1-M12) *TL: FFRD, IBG, CAU; Contributors: EURORDIS, RSU, RDB.* T24.2. aligns with GO:3; SO:3,5; OO:3.
This task aims at unlocking the full potential of UCs, to detect latent and unknown RD-related assets in these countries, additional patient populations and convert it into added value for the ERDERA. **In Year 1** of ERDERA, the measures to identify RDs with particular (geographic) incidence, distinctive critical mass, and infrastructural resources will be implemented by FFRD, IBG, CAU, and other contributors, in close collaborations with national entities, NMGs and scientific societies. In addition, synergies with the JARDIN, EURORDIS, HNN3.0 (Health NCPs), NFP4EU (Health NFPs), and the NCP_WIDERA.NET will be started to get further support for the identification of UCs added value.

ST24.2.1. Building synergies with JARDIN, EURORDIS, HNN3.0, NFP4EU, NCP_WIDERA.NET and others *Contributors: FFRD, IBG, CAU, EURORDIS, RSU, RDB.*
Within this ST, a consolidated interaction effort with networks in the area of Health will be implemented, in order to share contacts, data, and good practices regarding UCs, avoiding the duplication of efforts.

ST24.2.2. Identify UC assets, populations, expertise of value to R&I efforts *Contributors: FFRD, IBG, CAU, EURORDIS, RSU, RDB.*
Within this ST, information will be collected and presented, detailing UC assets, populations, expertise of value to R&I efforts (including infographics).

T24.3. Support actions to improve UC participation in all ERDERA activities (M1-M12) *TL: AICIB, IMGGE; Contributors: TUBITAK, RIF, ZonMw, VULSK, EURORDIS, CVBF, HRB.* T24.3. aligns with GO:3; SO:5.
This task aims to identify actions to effectively increase participation of the UCs RD community in ERDERA, and the funds available for both UCs and ERDERA partners in general. **In Year 1** of ERDERA, AICIB and IMGGE, together with task contributors, will develop guidelines for promoting the inclusion of UCs in ERDERA funded actions, e.g. JTCs, Networking Calls, and others, in coordination and dialogue with the workstream leads. The outputs of the needs mapping (ST 24.1.1), lessons learnt from EJPRD, EURORDIS surveys, and other relevant initiatives will be taken into consideration, and new measures that may increase UCs participation proposed. Baseline figures will be established, and targets proposed for levels of participation in these activities. In addition, measures and guidelines used in the Widening programmes (e.g., Twinning, Excellence Hubs, Hop-on) will be analysed and an adaption of these used in ERDERA activities when appropriate. Moreover, the possibility to access additional financial support (e.g., EU Widening programmes, structural funds) to increase UC participation in ERDERA and leverage the available funds will be explored and a proposal of measures to be implemented will be discussed with ERDERA coordination and the ERDERA workstream coordinators and will be highlighted to NMGs.

ST24.3.1. Identify actions to increase participation in ERDERA, and targets for participation *STL: AICIB; Contributors: IMGGE, HRB, ZonMw, VULSK, EURORDIS, TUBITAK, RIF.*
Within this ST, indications, and recommendations on procedures to be implemented, in order of increasing UCs participation in ERDERA funded actions, will be developed and presented.

ST24.3.2. Propose measures and guidelines to be implemented in ERDERA to increase UCs integration and leverage the ERDERA budget *STL: AICIB; Contributors: IMGGE, HRB, ZonMw, VULSK, EURORDIS, TUBITAK, RIF.*

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Within this ST, a list of procedures and measures will be developed and presented, to increase UCs participation in ERDERA and leverage its budget.
Additional deliverables *(additional to those included in part B of the proposal)*
None

Set of Activities Number	**25**		**Start Date or Starting Event**			**M1: September 2024**	
Set of Activities Title	**ERDERA Global Collaborations**						
Short name of participant & (No)	IOR (74)	SU (142)	ZonMw (7)	RDI (34)	FFRD (29)	EUROR DIS (26)	ISCIII (72)
Person Months	1.0	0.4	3.0	4.0	30	0.4	0.4
Short name of participant & (No)	AICIB (32)	AUMC (20)	ASU-FC (39)	HSJD (150)	CAU (123)	RCC* (162)	CIHR* (153)
Person Months	0.4	0.4	3.4	2.4	0.4		
Short name of participant & (No)	CHEO-RI* (152)	TEAMIT (2)					
Person Months		6					
Start month	M1		**End month**		M12		
**Associated partners providing in-kind contribution*							

State of the art behind this WP

In spite of the significant developments made in the RD field in recent years, it is important to acknowledge that a substantial portion of the global population, with over 300 million individuals worldwide living with RDs and more than 30 million RD patients in Europe, continues to confront unmet needs. This emphasizes the importance of fostering international collaboration in RDs research. Through collaboration, we can reduce the fragmentation of resources, harness the collective knowledge and expertise, and facilitate the exchange of information and data, ultimately leading to improved diagnosis and the development of new and novel treatments. Furthermore, the 2021 United Nation General Assembly Resolution on "Addressing the challenges of persons living with a RD (PLWRDs) and their families"[20] specifically encourages countries on strengthening international collaboration, coordinating research efforts, as well as the sharing of data.

In 2011, IRDiRC was established as a pivotal organization, bringing together diverse stakeholders dedicated to addressing the challenges of RDs research. The Consortium comprises RD research funders, patient alliances, researchers, clinicians, regulatory scientists, and industry representatives from Europe, North and Latin America, Africa, Asia, and Australia. With its global reach and collaborative approach, IRDiRC plays a vital role in driving research efforts within the field by providing a forum for global RD stakeholders to gather, collectively work under a common vision, and seize opportunities to advance RD research. In recent years, the IRDiRC Scientific Secretariat (SciSec), responsible for supporting IRDiRC's activities and functions, became a part of the EJP RD. This strategic alignment ensures synergies between IRDiRC and EJP RD, facilitating a coordinated approach to RD research and innovation. Moving forward, the SciSec will be seamlessly integrated into ERDERA, amplifying the impact and effectiveness of global collaborative efforts. The integration of the SciSec into ERDERA will further strengthen the ability of this Partnership to drive transformative change on a global scale.

The European CRN for RDs will be a new infrastructure developed in ERDERA. Building this new CRN and collaboration with other CRNs beyond Europe is very important for PLWRDs, as only 5%

of RDs have therapies, and many PLWRDs are still in need for timely and optimal diagnosis. Recognizing the existence of similar CRNs and initiatives in various continents, IRDiRC and EJP RD jointly organized a meeting in December 2022. The purpose of this gathering was to establish connections and lay the groundwork for an International CRN. This start of collaboration will be extended in ERDERA. Fostering closer collaboration and aligning research strategies within Europe among the ERNs and research teams working on RD presents another opportunity to alleviate fragmentation of budget and enhance knowledge and expertise. As ERNs are important actors in clinical research, ERDERA will enable discussions and cross-talks between ERNs on their research strategies and will encourage the discussions with other ERDERA stakeholders to create mutual benefit in aligning research strategies.

In addition, aligning capacity building and education activities will contribute to the objective of supporting a new generation of young scientists to continue the drive in R&I in RDs. Creating avenues for shared learning, exchanging best practices, and fostering interdisciplinary collaboration will lead to improved research outcomes and a more cohesive RD research community across Europe and around the world.

By supporting the SciSec, creating global strategic alliances, establishing the CRN, and promoting collaboration among universities, ERNs, and other stakeholders, ERDERA aims to create synergies, streamline efforts, and foster a culture of cooperation in the RD research landscape that transcends geographical boundaries. These initiatives will enable the pooling of resources, knowledge, and expertise, ultimately accelerating research advancements and benefiting patients worldwide.

Methodology

- **Patient-centred approaches**: Involving patient representatives in the discussion and shared decision-making process to ensure that their voice and perspectives are prioritized in the shaping of alliances and collaborations.
- **Establishing Working Groups:** Forming working groups composed of experts from different countries that can facilitate collaboration, knowledge exchange, and implement joint events or research efforts. These groups can focus on specific themes or topics (e.g. Mapping of potential strategic partners and already existing university alliances, Mapping of funding research priorities, Mapping of RD CTs, etc.) enabling the pooling of expertise and resources globally.
- **Creating the ERN Living lab:** A platform/discussion forum for cross-fertilization between ERNs and researchers and clinical experts.
- **Establish International Strategic Alliances:** Creating strategic alliances through MoU or Partnership agreements with European and global programs, projects, initiatives, universities, and patient organizations. Such alliances enable the sharing of vision, expertise, and infrastructure towards joint research endeavours.
- **Workshops and Conferences:** Organizing joint workshops and conferences with IRDiRC can bring together researchers, clinicians, patients and families, industry representatives, and other stakeholders from different countries. These events can provide opportunities for networking, discussing research findings, and identifying potential collaborative projects. Participation to strategic academic or learned societies meetings may provide as channels to raise awareness and attract collaborations.
- **Alignment with IRDiRC Activities:** Leveraging existing IRDiRC platforms and activities, such as task forces and working groups, can help synchronize efforts and streamline collaborative projects.

Collaborations needed with other activities in ERDERA are:

- Workstream on Funding
- Workstream on CRN
- WP2 Communication
- WP20 Education and Training in RD Research

Objectives

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

The main objective of this WP is to foster international collaboration and to align and promote research among international RD research stakeholders.

Specific objectives for Year 1:

- Initial mapping of potential international strategic alliances.
- Building a dedicated Working Group to help with identifying additional international strategic alliances.
- Preparation of model MoUs and Partnership agreements.
- Facilitating a smooth transition between INSERM and FFRD regarding the coordination of the SciSec and ensuring the fulfilment of IRDiRC's needs and requests from the various bodies.
- Gather materials and outputs from the first International CRN Conference and develop potential themes based on recommendation of the IRDiRC CRN Task Force. Engage and liaise external stakeholders in the USA who expressed interest to organise a CRN Conference during Year 1.
- Dissemination of ERDERA to ERN members.
- Build the governance of the ERN Living Lab and identification of stakeholders.

Description of Programmed Activities

T25.1. Strategic Alliances (M1-M12) *TL: INSERM_IT-GGB, SU, ZonMw; Contributors: RCC*, CIHR*, RDI, EURORDIS, FFRD, ISCIII, AICIB, CAU, AUMC, ASU-FC, HSJD.* T25.1. aligns with GO:1-3; SO:4,5; OO:2,3,5.

This task, in collaboration with WP1 and other Partnership WPs, aims to foster effective international collaboration and maximize outreach of ERDERA results through strategic alliances. To ensure effective international collaboration, while avoiding overlap with IRDiRC activities, **the following actions in Year 1 will be performed to establish strategic alliances with European and global RD programmes, projects, and initiatives.**

ST25.1.1. Research and Mapping of Strategic Partners *STL: INSERM_IT-GGB, SU, ZonMw; Contributors: RCC*, CIHR*, RDI, EURORDIS, FFRD, ISCIII, AICIB, CAU, AUMC, ASU-FC, HSJD.* INSERM_IT-GGB will be performing the first screening of potential international strategic alliances with European and international programs, projects (including EJP RD and ERDERA funded projects and initiatives) that has not been identified in the SRIA of the Partnership or in the EJP RD. In parallel, Sorbonne University will be performing the mapping of potential international university partners. In these screening and mapping activities potential partners will be identified that have a similar mission, complementary expertise, or shared interests in specific RDs research areas, ensuring diversity in the research and outreach efforts, and a broad geographical, cultural, and socio-economic inclusivity. The advantages, benefits, potential risks, and harms associated with establishing alliances and partnerships will be clearly defined and documented to support decision-making regarding partnerships and strategic alliances. After the two parallel mappings have been accomplished and the draft document on advantages/ benefits, etc., has been written, a Working Group composed of the TLs and contributors will be established to further develop the collated list of identified international strategic partners and discuss the draft document on advantages/benefits, etc. **The contributors have already suggested many European and international programmes/initiatives in the preparation of this ST that will be explored further in Year 1 of the Partnership.** Also, members of IRDiRC will be contacted for recommendations.

ST25.1.2. Establishment of Strategic Alliances and Partnerships *STL: INSERM_IT-GGB, Sorbonne university, ZonMw; Contributors: RCC* (Australia), CIHR* (Canada), RDI, EURORDIS, FFRD, ISCIII, AICIB, CAU, AUMC, ASU-FC, HSJD.*

Members of the Working Group will be facilitator and performer of partner matchmaking, identifying specific topics and opportunities for collaboration with the different ERDERA WPs. These partnerships will be established through MoUs or Partnership agreements with the support of INSERM_IT-GGB, in which the shared objectives, responsibilities, resources, and expected outcomes of the collaboration with the specific partner will be stated. **Model MoUs and partnership agreements will be prepared in Year 1 that can be adjusted dependent on the kind of strategic**

alliances that will be established.

ST25.1.3. Review of progress and outcomes of Established Strategic Alliances and partners *STL: INSERM_IT-GGB, ZonMw, SU; Contributors: RCC*, CIHR*, RDI, EURORDIS, FFRD, ISCIII, AICIB, CAU, AUMC, ASU-FC, HSJD, UKHD, UT.*
INSERM_IT-GGB will provide support to the Working group in organizing regular virtual meetings to discuss progress, share updates, and address any challenges or opportunities that arise in preparing and establishing strategic alliances with ERDERA.

T25.2. Support to IRDiRC Scientific Secretariat (M1-M12) *TL: FFRD; Contributor: TEAMIT.* T25.2. aligns with GO:1-3; SO:4-5; OO:3,5.
Year 1 will be dedicated to facilitating a smooth transition between INSERM and FFRD regarding the coordination of the Scientific Secretariat (SciSec). The overall objective of the SciSec will be to ensure the fulfilment of IRDiRC's needs and requests, assisting various bodies such as the Consortium Assembly, Constituent Committees, Scientific Committees, Operating Committee, Task Forces, and Working Groups, optimizing their complementary activities. The SciSec will organize and participate in bi-weekly meetings with the Chair and Vice Chair of IRDiRC, monthly meetings with the Operating Committee, and regular meetings (every 1-3 months) with IRDiRC committees. The SciSec will also organize and coordinate two Consortium Assembly in-person meetings, including a joint meeting with the Scientific Committees, and online meetings of the Consortium Assembly. The SciSec will support IRDiRC members in building a new roadmap of activities and facilitate the implementation, development, and dissemination of these activities. A maximum of four new activities will be supported by the SciSec. Task Force meetings are organized monthly and involve the active participation of the SciSec. The SciSec will jointly work with TEAMIT (WP2) to manage the communication and dissemination of IRDiRC activities through different communication channels (website and social media). Finally, the SciSec will manage administrative tasks and coordinate turnover and new membership within IRDiRC and its committees.

T25.3. Promote the International Dimension of the CRN of ERDERA by building global networks among CRNs and patient organizations (M1-M12) *TL: RDI, INSERM_IT-GGB; Contributors: AICIB, AUMC, c4c-S, UKHD, UT; CHEO-RI*; RCC*.* T25.3. aligns with GO:2,3; SO:3-5; OO:2,3,5.
To pave way to the promotion of European CRN and international networking, RDI and INSERM_IT-GGB will begin gathering materials and outputs from the first International CRN Conference which took place in December 2022. The materials include the programme, speakers, participant list, presentations, and any feedback survey results. The materials will be analysed and form a baseline for the organisation of the new CRN Conference in ERDERA Year 2. Task contributors will provide a list of known CRNs from their networks. Additional source of information such as the recommendation of the IRDiRC CRN Task Force will be considered for developing themes for networking or matchmaking. **RDI will engage and liaise external stakeholders from National Institute of Health (NIH), USA who expressed interest to organise a CRN Conference during Year 1.** If the organisation of an USA edition of CRN conference will be agreed by external partners, effort will be made to share information on existing CRNs and take part in scientific programme committee.

T25.4. Alignment with the Research strategies of the European Reference Networks (M1-M12) *TL: ASU-FC, HSJD; Contributor: IOR.* T25.4. aligns with GO:3; SO:1,4,5; OO:3-5.

ST25.4.1. Alignment and integration of the strategic research roadmap of the ERNs in the ERDERA and beyond *STL: ASU-FC, HSJD; Contributor: IOR.*
The 24 ERNs are the vectors of clinical care and research within the EU. They were created by the European Commission to facilitate interaction between expert medical teams in all fields of RDs, sharing of practices and close interaction with patient advocates. **In Year 1**, all 24 ERN coordinators will be involved in a smooth transition of the activities performed under the ERICA project (that will end in early 2025) and a collaborative identification of transversal and disease-specific priorities emerging by the medical teams, members of the ERNs. **Furthermore, the ERDERA priorities will**

be analysed, disseminated, presented, and discussed between the ERN members in Year 1, aiming to identify common points of actions and the ways, as well as necessary support, to achieve them.

ST25.4.2. Creation of the ERN Living lab (ERN-LL), a platform for cross-fertilization between researchers and clinical experts *STL: ASU-FC, HSJD; Contributor: IOR.*
Involvement of the medical teams of experts already at the front of clinical and fundamental research within the EU are crucial to the success of the ERDERA aims. **In Year 1**, a platform "ERN Living Lab' will be created through building a governance structure (Living Lab Board) and identification of stakeholders. The Living Lab Board will contribute to the setting of a general outline of plan of actions, including ensuring a regular communication between the ERNs as networks and the individual experts in their respective fields, thus facilitating the translation of projects to concrete actions at the service of the patients.

ST25.4.3. **Alignment of the Joint Action for Integration of ERNs (JARDIN) with ERDERA** *STL: IOR.*
The ERNs also have as a mission to support the development of well-structured national networks for RDs. The EC funded JARDIN project, to be launched in parallel with ERDERA, offers a unique opportunity for comprehensive approaches involving both the Member States and medical teams collaborating with the ERN members. **In Year 1**, priorities of JARDIN will be identified and their alignment with ERDERA actions will be discussed between the ERN members.

Additional deliverables *(additional to those included in part B of the proposal)*

None

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2.1.3.2. List of programmed activities

Table 2.3.b: AWP Set of Activities

Activity No.	Activity Title	Short name of lead participant and (No.)	Person-Months	Start Month	End month
WP1	Coordination & Management	INSERM	90	M1	M12
WP2	Communication & dissemination	Teamit	30	M1	M12
	Communication & dissemination	INSERM		M1	M12
WP3	Joint Transnational Calls for collaborative research projects	ANR (4)	3.25	M1	M12
	Joint Transnational Calls for collaborative research projects	DLR (3)	14.75	M1	M12
WP4	Clinical trial call management	FTELE (5)	1.6	M1	M12
	Clinical trial call management	DLR (3)	1	M1	M12
WP5	Networking to share knowledge on research	LMT (6)	1.25	M1	M12
	Networking to share knowledge on research	ZonMw (7)	2.00	M1	M12
WP6	Diagnostic Data Availability	UT (8)	27	M1	M12
	Diagnostic Data Availability	UTartu (9)	24	M1	M12
	Diagnostic Data Availability	CNAG (10)	15	M1	M12
WP7	Genome re-analysis research pipeline	CNAG (10)	27	M1	M12
	Genome re-analysis research pipeline	SRUMC (11)	33	M1	M12
WP8	Genomic innovation to shorten time to diagnosis	SRUMC (11)	24	M1	M12
	Genomic innovation to shorten time to diagnosis	TUM (12)	21	M1	M12
WP9	Real World Data	UKHD (13)	50	M1	M12
	Real World Data	C-Path (14)	24	M1	M12
WP10	Clinical Outcome Assessment	ICS-VHIR (15)	21	M1	M12
	Clinical Outcome Assessment	UKHD (13)	21	M1	M12
WP11	ATMPs	INSERM ART-ARNm (1)		M1	M12

	ATMPs	UKHD (13)	9	M1	M12
WP12	N-of-Few Approach	LUMC (16)	6	M1	M12
WP13	Rare Disease Virtual Platform (RD-VP) finding and accessing the data ecosystem	INSERM_Orphanet (1)	8.62	M1	M12
	Rare Disease Virtual Platform (RD-VP) finding and accessing the data ecosystem	INSERM_Orphanet (1)	13.28	M1	M12
WP14	Data readiness services	LUMC (16)	8	M1	M12
	Data readiness services	UPM (18)	9	M1	M12
WP15	Data sharing and analysis services	UMCG (19)	26	M1	M12
	Data sharing and analysis services	CNAG (10)	13.5	M1	M12
WP16	Knowledge bases and ontologies for RD research	AUMC (20)	10	M1	M12
	Knowledge bases and ontologies for RD research	UM (21)	12	M1	M12
WP17	Initiation of Mentoring process and feasibility study for consultancy services	EATRIS (22)	11	M1	M12
	Initiation of Mentoring process and feasibility study for consultancy services	FGB (23)	3	M1	M12
WP18	Regulatory support service	FGB (23)	20	M1	M12
	Regulatory support service	EATRIS (22)	14	M1	M12
	Regulatory support service	Pfizer* (161)	1	M1	M12
WP19	Methodological support	APHP (24)	12	M1	M12
	Methodological support	UHASSELT (25)	12	M1	M12
WP20	Education and Training on RD Research	EURORDIS (26)	21.4	M1	M12
	Education and Training on RD Research	VULSK (27)	14	M1	M12
WP21	Technology accelerator	UC (28)	19.08	M1	M12
	Technology accelerator	Pfizer* (163)	3.80	M1	M12
WP22	Public-private collaboration accelerator	FFRD (29)	12	M1	M12
	Public-private collaboration accelerator	AFM (30)	12	M1	M12
WP23	NMG promotion and national alignment	INSERM (1)	0	M1	M12
	NMG promotion and national alignment	CCUH (31)	8	M1	M12
	NMG promotion and national alignment	UNEW (85)	12	M1	M12
WP24	Fostering engagement of underrepresented countries in ERDERA	AICIB (32)	9.87	M1	M12

	Fostering engagement of underrepresented countries in ERDERA	IMGGE (33)		M1	M12
WP25	ERDERA Global Collaborations	ZonMw (7)	3	M1	M12
	ERDERA Global Collaborations	RDI (34)	4	M1	M12
			626		

2.1.3.3. List of annual deliverables

Table 2.3.c: List of Additional Deliverables (*additional to those included in AWP of the proposal)*

Deliverable No	Deliverable Name	Activity No.	Lead Participant Short Name & (No.)	Type	Dissemination Level	Delivery Date
D4.1	Other documents related to CT call text and procedures.	WP4	FTELE (5)	R	SEN	Within Year 1
D6.1 - D6.6	Report on Data Availability Committee establishment and organigram	WP6	UT (8)	R	PU	M6
	List of standards and minimum quality criteria for data submission	WP6	UT (8)	R	PU	M6
	List of prioritised submitting centres, including early adopters of the federated approach	WP6	UT (8)	R	PU	M12
	Identification of additional requirements and needs of the CRN Diagnostic Research workstream to be developed in Data Management System	WP6	UT (8)	R	PU	M3
	10,000 harmonised datasets from centralised and/or federated approaches available in the CRN Diagnostic Research Ecosystem	WP6	UT (8)	OTHER	PU	M12
	Data collation toolkit	WP6	UT (8)	OTHER	PU	M3
D10.1 - 10.3	Design of respective input method (structured interview,	WP10	ICS-VHIR (15), UKHD (13)	R	PU	M12

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	focus group, survey) completed and pilot tested					
	Top-ranked CAOs for further validation selected for each target disease	WP10	ICS-VHIR (15), UKHD (13)	R	PU	M12
	Regulatory strategy for each target disease established	WP10	ICS-VHIR (15), UKHD (13)	R	PU	M12
D15.1 - 15.2	Draft proposal for the application of federated data processing and analysis services in ERDERA.	WP15	UPM(18), CNAG(10), UMCG(19)	OTHER	PU	M12

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

2.2. Participation in Annual Work Programme activities

1-INSERM

Name of the legal entity	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE

Expertise, available infrastructure(s)

INSERM is the coordinator of the European Joint Programme on Rare Diseases and will be the coordinator of ERDERA. INSERM has strongly contributed to the development of tools on the virtual platform through the Orphanet services. INSERM is the major actor in the implementation of the French genomic medicine initiative analysis platform and will provide federative access to rare disease genomic data through Inserm-CAD. INSERM will also co-leads tasks related to the development and dissemination of Clinical Utility tools based on the expertise developed through its contribution in EU Solve-RD project. It has also highly experienced staff and state-of-the-art equipment for the design and production of mRNA and target delivery that will be a major asset for the development of innovative treatments based on mRNA nanoparticles. INSERM will also contribute to the design of novel clinical trials through the recognized methodological expertise in digital health and adaptative clinical trial designs. Hélène Dollfus, MD-PhD (U1112), has strongly contributed to the development of ERN and in particular the ERN-EYE. She will bring her expertise in medical and functional genomics.

Main tasks in the project:

Team IT-GGB:

Coordinator

Leader: **WP1.0**; Task1.1; Task1.2; Task11.3; **WP23.0**; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task25.1; Task25.3;
Contributor: Task1.3; Task1.4; Task1.5; Task2.1; Task2.2; Task2.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;

Team ART-ARNm

Leader: WP11.0; Task11.3; Task21.3;
Contributor: Task11.2; Task11.4; WP21.0; Task21.2;

Team CAD

Leader: Task6.2; Task7.2; Task15.2;
Contributor: WP6.0; Task6.3; WP7.0; Task7.1; Task7.4; Task15.3;

Team Orphanet

Leader: WP13.0; Task13.1; Task16.1; Task16.2; Task16.5;
Contributor: Task7.2; Task13.2;

Team Target (Nantes)

Contributor: WP21.0; Task21.1; Task21.5;

Team U1138

Leader: Task19.1; Task19.2;
Contributor: Task9.5;

Team U974

Leader: Task7.4; Task16.3;
Contributor: WP7.0; Task7.1; Task7.2; WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;

Team U1112 (UNISTRA)

Contributor: Task6.2; Task6.3; Task7.1; Task7.3; Task9.4;

2 - TEAMIT

Name of the legal entity	TEAM - IT RESEARCH SL

Expertise, available infrastructure(s)

Teamit Research (TEAMIT) is a research management organisation, building strong public-private partnerships and providing transversal expertise for impactful health science. It aims to empower collaborative research and innovation for a healthier future.

TEAMIT supports research projects by providing extensive knowledge and experience in the areas of project and scientific management, communication, multi-stakeholder engagement, regulatory science, real world evidence, training and education, quality, risk management, sustainability and exploitation. TEAMIT collaborates with partners from the entire health ecosystem to ideate and implement research and innovation initiatives. It works with academia, clinical centres, health industry, SMEs, patient and civil society organisations, regulatory, funding bodies, policy makers, regional and national authorities.

Within ERDERA, TEAMIT will contribute to the Partnership transversal activities (WP1, WP2). Firstly, by leading WP2 – Communication, it will apply its expertise and experience in driving Communication efforts in multiple large research projects (IMI EU-PEARL, IMI RESCEU, IMI PROMISE, HE Fibrotarget). TEAMIT will work to generate awareness on the Partnership, amplify dissemination and acceptance of research outputs, promote ERDERA's activities and calls and facilitate stakeholder engagement. Moreover, TEAMIT will contribute project management support in WP1, by managing the EC reporting process, the elaboration of the Annual Work Plans and supporting the Governing Board meetings.

Main tasks in the project:

Leader: **WP1.0**; **WP2.0**; Task2.1; Task2.2; Task2.3;

Contributor: Task1.1; Task1.2; Task1.3; Task1.4; Task25.2; SubTask25.2.1; SubTask25.2.2; SubTask25.2.3;

3 - DLR

Name of the legal entity	DEUTSCHES ZENTRUM FUR LUFT - UND RAUMFAHRT EV

Expertise, available infrastructure(s)

DLR is a non-governmental, non-profit German research organisation. Its Project Management Agency DLR-PT is mandated by the Federal Ministry of Education and Research (BMBF) and other ministries for implementation and management of governmental programmes for research funding. On behalf of BMBF, the "health research" department of DLR-PT has already participated in E-Rare1-3 and EJP RD and managed 4 Joint call secretariats. DLR-PT is also engaged in several other ERA-Nets, JPIs and European Partnerships and manages a large and growing number of transnational calls, and is serving as call secretariat for many of them. DLR-PT is currently co-leading Pillar 1 for research funding in EJP RD and is very engaged in the management of the programme. DLR-PT will co-lead the RD funding workstream and the WPs on joint transnational calls and clinical trial calls. It will also be responsible for hosting 2 joint call secretariats.

Main tasks in the project:

Leader: **WP3.0**; Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Task3.3; **WP4.0**; Task4.1;

Contributor: Task1.3;

4 - ANR

Name of the legal entity	AGENCE NATIONALE DE LA RECHERCHE

Expertise, available infrastructure(s)

The French National Research Agency (ANR) was established to fund best basic/applied research, in particular in the biomedical field, SSH and interdisciplinary research topics linked to health. ANR's mission is also to strengthen international cooperation by contributing in particular to the funding of international consortia in partnership with other funding agencies in Europe and beyond. ANR participated in diverse European initiatives such as ERA-nets, JPIs, Art. 185 etc.... ANR was the coordinator of E-Rare-3 and co WP or task leader under EJP RD.

ANR will co-lead WP3 on the joint transnational calls and will thus be part of the ExCom. ANR will be in charge of the task on topic selection as under EJP RD, at least one call secretariat for the JTCs and contribute to the tasks on the monitoring of projects, patients engagement, NSS activities and support the communication/dissemination activities.

Main tasks in the project:

Leader: **WP3.0**; Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Contributor: Task1.3; Task3.3; Task5.1; Task5.3;

5 - FTELE

Name of the legal entity	FONDAZIONE TELETHON ETS
Expertise, available infrastructure(s) Fondazione Telethon (FTELE) is an Italian non-profit organization that has been supporting bio-medical research on rare and genetic diseases for more than 30 years. The vision of FTELE is to translate research results into therapies available to patients. Over the years Telethon Foundation has invested around 660 euro million funding almost 3000 research projects involving more than 1700 scientists. Every year Telethon Foundation launch a call for projects in the field of RD research open to all Italian not for profit research centres (including university and public hospitals). Moreover Telethon runs 2 research institutes, the Telethon Institute for Genetic Medicine (TIGEM) and the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget). In collaboration with pharmaceutical industries, FTELE research was developed up to marketing authorization resulting in 2 ex-vivo gene therapy products approved by the EMA (Strimvelis and Libmeldy). Since 2023 FTELE is the marketing authorization holder of Strimvelis.	
Main tasks in the project: Leader: Task3.1; **WP4.0**; Task4.1; Task4.2; Task4.3; SubTask4.3.1; SubTask4.3.2; **WP11.0** Contributor: Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; WP21.0; Task21.4;	

6 - LMT

Name of the legal entity	Lietuvos mokslo taryba
Expertise, available infrastructure(s) LMT is the main research funding body in the country executing competitive funding to the national research and higher education institutions for R&D using state budget, EU funds and other resources. We are developing and implementing national funding programmes, as well as participating in the international cooperation programmes and have expertise in such programme management taking different roles and taking part in various activities (see section IV). Participation and contribution in the joint funding (preparation and launch of transnational calls for research projects) and other relevant transversal activities; taking the role of the WP lead dedicated to the funding instrument for the networking and knowledge sharing. Involvement in the task dedicated to the Networking Support Scheme: preparation and launch of open calls to third parties to apply for funding of networking events, taking part in call secretariat work and the activities to ensure process quality.	
Main tasks in the project: Leader: **WP5.0**; Task5.1; Task5.2; Task5.3 Contributor: Task1.3; Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

7 - ZonMw

Name of the legal entity	ZORGONDERZOEK NEDERLAND ZON
Expertise, available infrastructure(s) ZorgOnderzoek Nederland (ZON/ZonMw) is an independent self-governing organisation with the Dutch Ministry of Health, Welfare and Sport and Dutch Research Council as important contractors. ZonMw programmes and funds health research and innovation in care, and facilitates the utilisation of knowledge to solve scientific and societal issues concerning care, health and well-being. Furthermore, ZonMw takes part in several ERA-Nets, JPIs, Art 185 programmes and European Partnerships. In the EJP RD, ZonMw is coleader of the Pillar "Research funding" and funds research in joint transnational calls. Furthermore, ZonMw is WP leader on the Networking Support Scheme and hosts this call secretariat. Partnerships. ZonMw will be co-leader of the Workstream (Inter)national collaboration, co-leader of the WP on Global collaboration and co-leader of the WP on networking to share knowledge, including hosting the secretariat for this support scheme. ZonMw will fund research projects in joint transnational calls.	
Main tasks in the project:	

Leader: **WP5.0**; Task5.1; Task5.2; Task5.3; **WP25.0**; Task25.1 Contributor: Task1.3; Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Task3.3; WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3; Task24.3;

8 - UT

Name of the legal entity	EBERHARD KARLS UNIVERSITAET TUEBINGEN
Expertise, available infrastructure(s) UT is a world-leading cluster of expert institutions focusing on research of rare diseases in particular rare neurological disease, bringing together the expertise and methodologies from the Institute of Medical Genetics and Applied Genomics, the Centre for Rare Disease, the Hertie-Institute for Clinical Brain Research (HIH), the German Centre for Neurodegenerative Diseases (DZNE). UT has been coordinating leading European RD projects such as Solve-RD, NeurOmics, EUROSCA and 1M1M. UT is the coordinator and leading centre of the ERN-RND (European Reference Network on Rare Neurological Diseases). This ERN establishes a large patient-centred network to address the needs of patients with RND of all age groups, with or without a definite diagnosis, by implementing an infrastructure for diagnosis, evidence-based management, treatment and collection of patient data.	
Main tasks in the project: Leader: **WP6.0**; Task6.1; Task6.3; Task7.1; Task8.2; Task9.5; Task12.2; Task12.3; Task12.5; Task13.2 Contributor: Task6.2; WP7.0; Task7.2; WP8.0; Task8.1; Task8.3; Task8.4; Task8.5; Task9.3; Task10.1; Task10.2; Task12.1; Task12.4; Task20.3; SubTask20.3.1; SubTask20.3.2; Task25.3;	

9 - UTartu

Name of the legal entity	TARTU ULIKOOL
Expertise, available infrastructure(s) UTartu is a leading research intuition in Estonia in the field of RD discovery, care and treatment. UTartu is tightly connected with Tartu University hospital who is the only medical institution in Estonia to provide genetic testing, newborn screening and genetic counselling in a wide range of clinical indications and all age groups. UTartu is involved in H2020 B1MG (Beyond 1 Million Genomes), to support the EU Member State 1+ Million Genomes Initiative and the European Genomic Data Infrastructure (GDI). UTartu is actively collaborating in the field of rare diseases discovery with the Center of Mendelian Genomics at Broad Institute MIT Harvard.	
Main tasks in the project: Leader: **WP6.0**; Task6.1; Task6.2 Contributor: Task20.3; WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;	

10 - CNAG

Name of the legal entity	CONSORCIO PARA LA EXPLOTACION DEL CENTRO NACIONAL DE ANALISIS GENOMICO
Expertise, available infrastructure(s) The CNAG sequences >20,000 exomes/genomes from RD patients per year, and has experience in NGS data management, quality control and analysis. The Bioinformatics Unit, led by Dr Beltran, includes 20 highly experienced members and develops user-friendly pipelines and tools for NGS data analysis and interpretation. Dr Beltran leads the development of the RD-Connect GPAP, participates in several RD EU (H2020 Solve-RD, H2020 EJP-RD, H2020 B1MG, IMI Screen4Care,) and national (1000 PERIS URD-Cat, IMPaCT-Genómica) projects and co-leads the ELIXIR RD-Community. The Unit contributes to MatchMaker Exchange (IRDiRC/GA4GH) and Beacon initiatives (GA4GH, ELIXIR). CNAG will contribute to ERDERA by providing i) expertise and data processing to WP6 (WP co-lead) and WP7 (WP co-lead), ii) software and technical support to WP15 (WP co-lead) and iii) training support (co-lead task 20.3). To carry out these project activities, the unit has access to the CNAG and RD-Connect GPAP clusters (13,000/304 cores).	
Main tasks in the project:	

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Leader: **WP6.0**; Task6.1; Task6.2; **WP7.0**; Task7.1; Task7.2; WP15.0; Task15.3; Task16.3; Task20.3; SubTask20.3.1
Contributor: Task6.3; Task7.4; WP8.0; Task8.1; Task8.2; Task8.3; Task8.4; Task8.5; Task13.2; Task14.1; Task15.1; Task15.2;

11 - SRUMC

Name of the legal entity	STICHTING RADBOUD UNIVERSITAIR MEDISCH CENTRUM

Expertise, available infrastructure(s)
Radboudumc is one of largest (out of seven in total) University Medical Centres (UMCs) in The Netherlands with approximately 11,100 employees and 609 hospital beds. The combination of high-quality scientific research, patient care and education within one organisation is unique in the world. The strong interrelationship between science, patient care and education enables Radboudumc to deliver the best possible care, applying the latest insights in healthcare. Radboudumc, being organized this way, covers the whole spectrum from basic exploration of biological processes, through translational research and patient-related research, to epidemiological studies and clinical applications. This is an important source of care renewal. Conversely, observations in patients may generate new hypotheses to be explored with basic or experimental translational research, increasing our knowledge.
Radboudumc's mission is ‘to have a significant impact on healthcare’. Its activities help to improve healthcare and consequently the health of individuals and of society. Radboudumc believes it can achieve that by providing excellent quality, participatory and personalized healthcare, operational excellence and by working together in sustainable networks. Its frame of reference is always the individual patient, who is unique. Unique characteristics include not only the genetics, biology and physiology, but also the psyche, social environment and wishes, responsibility and capabilities of the individual. In the vision of Radboudumc, all patients participate in their own healthcare. Clinicians, researchers and patients work together to uncover the causes of diseases and find cures for them. In this way, participatory healthcare has become the focal point of patient care, education and research at Radboudumc.
Health and disease are based on underlying molecular and cellular mechanisms. Radboudumc offers many possibilities to translate knowledge on aetiology and development of diseases into clinical practice, in terms of susceptibility, prevention, diagnostics, prognosis and therapy for the patients concerned. Radboudumc combines knowledge from the two biomedical worlds, mechanism-based and evidence-based medicine, to create person-based medicine. In this way, the research at Radboudumc goes from molecule to man to population and back to man. Subsequently, the individual patient is always the starting and ending point of any research.
Research in the Radboudumc is conducted within the Radboud Institution for Medical Innovation. Researchers are working together to achieve a research environment that enables us to create societal impact and gain insights, while maintaining a sustainable organization that pays attention to the well-being of our researchers. In the near future our research will be conducted primarily in the context of research programs, each covering the full chain from bench to bedside, which are clustered in four research domains: 1) Discovery science BioMedTech; 2) Clinical science; 3) Health science; 4) MedTech & Data science.
1)Discovery science & BioMedTech: Researchers in this domain seek to gain a mechanistic understanding that encompasses a wide range of biological, psychological, and social mechanisms that are relevant for both prevention and medical care. Typically, research in this area is conducted through experimental work, which can also facilitate the development of novel interventions and therapies. (e.g.., BioMedTech).
2)Clinical science: In this domain, researchers strive to directly innovate healthcare by conducting clinical research with or near the patient. This involves both interventional as well as observational studies, or research focused on the organization of healthcare. n3) Health science: In this domain, researchers focus on studying (healthy) individuals and populations to gain a better understanding of the risk and resilience factors and the impact of preventive interventions. This domain also includes research of quality and sustainability of care.
4) MedTech & Data science: In this domain, researchers engage in the development and evaluation of sustainable medical technologies and data science that have the potential to be utilized in the realm of health and healthcare. Within the project, Radboudumc will play a leading role in the CRN, improving diagnosis of RD through reanalysis of existing exomes and genomes, multimodal data analysis and combining available data from genomes with those from the EHRs. Moreover, Radboudumc plays a leading role in the FAIRification of data from European resources through the data hub

Main tasks in the project:
Leader: **WP7.0**; Task7.1; Task7.3; **WP8.0**; Task8.2; Task8.3; Task9.1; Task14.1

Contributor: Task6.2; Task6.3; Task7.2; Task7.4; Task8.1; Task8.4; Task8.5; WP9.0; Task9.3; Task10.1; Task12.1; Task13.3; Task14.2; SubTask14.2.1; Task20.3; SubTask20.3.1; Subtask20.3.6; Task22.1;

12 - TUM

Name of the legal entity	TECHNISCHE UNIVERSITAET MUENCHEN
Expertise, available infrastructure(s) Prof Gagneur holds the chair for Computational Molecular Medicine at the Technical University of Munich, with a secondary affiliation at the Institute of Human Genetics, at the TUM university hospital (MRI-TUM). Gagneur develops computational methods for Rare Disease Diagnostics spanning non-coding variant interpretation and omics-based diagnostics. Gagneur is moreover PI at the German Human Genome Phenome Archive (GHGA, https://www.ghga.de/) in which he is leading the working group developing analysis workflows. GHGA is the infrastructure research backend for Germany's primary use research genomics data, as well as secondary use research genomics data (notably stemming from GenomDE: https://www.bundesgesundheitsministerium.de/en/en/international/european-health-policy/genomde-en.html).	
Main tasks in the project: Leader: **WP8.0**; Task8.4; Task8.5 Contributor: Task6.2; Task6.3; Task7.3; Task8.1; Task8.2; Task8.3; Task9.1; Task20.3;	

13 - UKHD

Name of the legal entity	UNIVERSITATSKLINIKUM HEIDELBERG
Expertise, available infrastructure(s) FS leads the clinical research workgroup on paediatric rare kidney diseases at UKHD, where several European and international rare kidney disease registries are coordinated that will be utilized for demonstrator projects in the ERDERA Outcomes Research WPs 9 & 10. FS will lead the Clinical Research Network workstream and the RWD WP 9 in ERDERA. SK is coordinator of registry-based observational studies for inherited metabolic disorders on a national (NBS 2020, NBS 2025) and European level (E-IMD, E-HOD, U-IMD). His department at UKHD provides newborn screening for >140,000 newborns annually and coordinates regional/national pilot studies for newborn screening. He will contribute an NBS demonstrator project to the population-based outcomes research task 2 of WP9. MRS is coordinator of the BMBF- and EJP-RD funded networks TreatHSP and PROSPAX that coordinate translational research and natural history studies in Hereditary Spastic Paraplegias and Spastic Ataxias. Longitudinal clinical and biomarker datasets from these networks will be utilized for demonstrator projects in the ERDERA Outcomes Research WPs 9 & 10. RS will (co-)lead RWD WP10 and contribute to tasks in WP9 and WP12.	**Expertise, available infrastructure(s)** FS leads the clinical research workgroup on paediatric rare kidney diseases at UKHD, where several European and international rare kidney disease registries are coordinated that will be utilized for demonstrator projects in the ERDERA Outcomes Research WPs 9 & 10. FS will lead the Clinical Research Network workstream and the RWD WP 9 in ERDERA. SK is coordinator of registry-based observational studies for inherited metabolic disorders on a national (NBS 2020, NBS 2025) and European level (E-IMD, E-HOD, U-IMD). His department at UKHD provides newborn screening for >140,000 newborns annually and coordinates regional/national pilot studies for newborn screening. He will contribute an NBS demonstrator project to the population-based outcomes research task 2 of WP9. RS is coordinator of the BMBF- and EJP-RD funded networks TreatHSP and PROSPAX that coordinate translational research and natural history studies in Hereditary Spastic Paraplegias and Spastic Ataxias. Longitudinal clinical and biomarker datasets from these networks will be utilized for demonstrator projects in the ERDERA Outcomes Research WPs 9 & 10. RS will (co-)lead RWD WP10 and contribute to tasks in WP9 and WP12.My lab and I possess and will contribute extensive expertise in the genetic engineering of efficient, specific and safe gene transfer vectors based on Adeno-associated virus (AAV) and bocavirus (BoV). This comprises a broad portfolio for the genetic diversification of viral capsid, genome and regulatory elements in a high-throughput manner, as well as an equally wide diversity of powerful and versatile strategies for the stratification of these libraries and the

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	enrichment of desired candidates ex vivo or in vivo (small and large animals). A central component is our team of dedicated and highly experienced bioinformaticians who are well trained in the storage, analysis and visualization of large biological data sets (DNA, RNA, protein). Moreover, we have access to all critical infrastructure required for this project, comprising a scientific large data storage system, an animal facility, various core facilities including single-cell RNA sequencing and a next-generation sequencing core.
Main tasks in the project: Leader: **WP9.0**; Task9.3; **WP10.0**; Task10.1; Task11.1; Task12.4; Task12.5 Contributor: Task9.2; Task9.4; Task9.5; Task9.6; Task10.2; Task12.1; Task12.2; Task12.3; WP21.0; Task21.1; Task25.3;	

14 – C-PATH

Name of the legal entity	CRITICAL PATH INSTITUTE STICHTING
Expertise, available infrastructure(s) Critical Path Institute (C-Path) is an independent, non-profit organisation created in 2005 following the U.S. Food and Drug Administration (FDA) release in 2004 of a report that launched the Critical Path Initiative. C-Path, in collaboration with health authorities, industry, academia, and patient groups, creates and/or refines drug development tools (DDTs) to speed up development of new treatments and diagnostics. All of the regulatory-endorsed tools generated by C-Path are made available to all stakeholders at no, or minimal, cost to speed up the availability of new medical products for patients in need. Our staff consists of professionals with strong program management, data science, data analytical, regulatory science and product development skills. C-Path solutions can include data resources, biomarkers, clinical outcome assessments, clinical trial simulators and other quantitative tools. These tools and solutions help de-risk decision making in the development and regulatory review process of novel medical products, owing to the active engagement of the regulators along the path to regulatory endorsement.	
Main tasks in the project: Leader: **WP9.0**; Task9.6; Task14.3 Contributor: Task9.4;	

15 - VHIR

Name of the legal entity	INSTITUT CATALA DE LA SALUT
Expertise, available infrastructure(s) Dr Mañú is the scientific director of the ERN-EuroBloodNet and coordinator of the European registration platforms for patients with rare haematological diseases, ENROL, and with rare anaemia disorders, RADeep. She coordinates WP3 at ERICA Consortium on "Patient reported outcomes". In addition, since 2023 she is a member of the Interdisciplinary Scientific Committee of the IRDiRC. Dr Mañú is leading in this proposal WP10 on "Clinical outcomes research" and also contributes in WP9. Dr Miguel Chillón is an ICREA researcher at VHIR with an extensive background in vector development for gene therapy. Former co-chair of Advanced Therapies of EATRIS (2015-2022), he has authored 14 patents and funded 2 spin-offs. Dr Ibane Abasolo is a senior researcher, head of the CB-DDT group and the FVPR/U20 technological platform at VHIR. She participates in several European projects developing nanoparticle-based treatments for rare diseases. Both, Dr Chillón and Dr Abasolo contribute to WP21.	
Main tasks in the project: Leader: **WP10.0**; Task10.2 Contributor: Task9.1; Task9.5; Task10.1; Task10.3; Task20.3; SubTask20.3.2; WP21.0; Task21.1; Task21.3;	

16 - LUMC

Name of the legal entity	ACADEMISCH ZIEKENHUIS LEIDEN
Expertise, available infrastructure(s)	

LUMC is a university medical centre for research, education and patient care. It offers state-of-the-art research facilities such as for genomics, proteomics, metabolomics, bioinformatics, FAIR data stewardship, stem cells, transgenic animals, and sample biobanks. It participates in the League of European Research Universities (LERU) education network. It participates in 8 ERNs, hosting two ERN registries. Prof Aartsma-Rus, co-leader of WP12, brings expertise from over 23 years of preclinical development of exon skipping therapies, leading (inter)national n-of-1 therapy developments (via IRDiRC, N-of-1 collaboratives, the Dutch Center for RNA Therapeutics). She engaged with regulators, patients and academics for Duchenne therapy development. Prof. Ahmed, Prof. Biermasz, and Dr Appelman-Dijkstra, leading endocrine specialists, contribute to the CRN stream. Ahmed and Appelman-Dijkstra lead the ENDO and BOND registries. Dr Santen, head of the LUMC Clinical Genetics department, has an extensive track record in rare disease research, identifying new causative genes, and a recognized expert of Coffin Siris syndrome, for which he recently completed a clinical trial. He submitted > 1800 datasets to solve-RD and will deliver high numbers of exome and genome datasets to the ERDERA diagnostic workstream. Dr Roos, co-leader of WP14, leads research of the LUMC Biosemantics group on analysing data with computable knowledge and implementing FAIR principles. He co-founded the FAIR principles that were initiated by the group's prof. Mons. Roos co-leads the ELIXIR rare disease community and the WP on FAIR implementation at source in the EJP RD. LUMC contributes to several tasks in the project pertaining to data analysis, FAIR implementation and development of AI, network analysis, and data integration.
Main tasks in the project: Leader: **WP12.0**; Task12.1; **WP14.0**; Task16.4 Contributor: Task6.2; Task6.3; Task9.3; Task9.5; Task12.2; Task12.3; Task12.4; Task12.5; Task13.2; Task13.3; Task14.2; Task14.3; Task16.5; Task20.1; Subtask20.1.1; Task20.3; Subtask20.3.6;

17 - UTWENTE

Name of the legal entity	UNIVERSITEIT TWENTE
Expertise, available infrastructure(s) I have previously co-chaired the IRDiRC WG on medical technology, have authored several publications on the overview of this field (currently under submission), am editing a special collection in this topic on OJRD, have participated in several congresses this year on this topic, and hosting session, am participating in the EC group of MDCG (definition of orphan device and incentives for orphan devices), and have a large network in this field, including a network of testing facilities of orphan devices. For other non-pharmacological treatments that are not devices, I have shaped and developed several research projects.	
Main tasks in the project: Leader: Contributor: Task13.1; Task14.1; Task20.3; Subtask20.3.6;	

18 - UPM

Name of the legal entity	UNIVERSIDAD POLITECNICA DE MADRID
Expertise, available infrastructure(s) Prof. Federico Alvarez is the coordinator of the projects GenoMED4ALL and TeNDER in H2020, Synthema in Horizon Europe which will provide technology and serve as a base for multi-omics and clinical data analysis and federated learning capabilities. Dr Mark D Wilkinson. has focused on creation and exploitation of semantic middleware for >25 years. He was author of several interoperability infrastructures including BIoMOBY and SADI/SHARE, which were widely deployed over bioinformatics tools worldwide. He is lead author of the primary FAIR Data Principles publication, which has been cited more than 10,000 times since its publication in 2016; FAIR was a core objective of the EJP-RD project, and is also at the core of the WP13/14/15 objectives in this ERDERA proposal. His role will be to ensure that all technological contributions in the project are aligned with the objectives of FAIRness, and will execute automated evaluations of FAIRness compliance.	
Main tasks in the project: Leader: Task13.3; **WP14.0**; Task14.2; Task15.3 Contributor: Task9.1; Task9.5; Task10.2; Task13.2; Task14.1;	

19 - UMCG

Name of the legal entity	ACADEMISCH ZIEKENHUIS GRONINGEN

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Expertise, available infrastructure(s) The UMCG (Academisch Ziekenhuis Groningen) is the second largest academic hospital in the Netherlands. The data methods and infrastructure work are planned at the Genomics Coordination Center (Prof Swertz) a 40fte bioinformatics core facility and big data stewardship hotel between the UMC/University of Groningen. GCC specializes in data catalogues, federated analysis, HPC genomics, and rare disease patient registries. All GCC software is open source and available as part of the MOLGENIS software platform for scientific data (http://www.molgenis.org). We are partner in BBMRI, ELIXIR, Health-RI. Within this project, GCC will be a main data analysis infrastructure partner, providing sample track and trace into WP6, innovative analysis pipelines using VIP in WP8, metadata federation in WP13 and WP14 as a task leader, and most importantly, co-leading WP15 to deliver high performance and federated analysis capability for CRN and funded projects.
Main tasks in the project: Leader: Task13.3; Task14.2; **WP15.0**; Task15.1; Task15.2 Contributor: WP6.0; Task6.1; Task6.2; Task6.3; Task7.1; Task7.2; Task7.4; Task8.2; Task13.2; Task15.3; Subtask20.3.6;

20 - AUMC

Name of the legal entity	STITCHING AMSTERDAM UMC
Expertise, available infrastructure(s) AUMC provides - state of the art access to institutional international RD infrastructures and personal expertise. Two ERNs as well as ERICA are coordinated from AUMC: Endo-ERN (prof. A. Pereira) and ERN-GUARD-HEART (prof. A. Wilde), as well as ERICA (also coordinated by prof. A. Pereira) that has created a platform that integrates all 24 ERNs - research and innovation capacity that significantly impact on the ERDERA and SRIA. AUMC participates in 20 ERNs (AUMC RD ECZA Office), with structured national (all representatives and coordinators are part of the Dutch National Mirror Group) and international RD networks (ERNs, ERICA, EJP RD). AUMC is foreseen to participate in the following ERDERA WPs: WP12; WP14; WP16; WP25. Prof. A. Pereira/ Dr Soeters are experts in CRN Non-Pharmaceutical Intervention Task Force. Prof. A. Pereira is professor of medicine, and head of the Department of Endocrinology & Metabolism. Dr Soetens is PI of the Metabolic Research unit focussed on feeding in health care. Prof. A. Wilde is professor in medicine and currently head of the Department of Clinical and Experimental Cardiology. Assoc Prof. R. Cornet is PI of the Reusable Health Data unit, and foreseen to lead the Knowledge Service Hub Stream (WP12-WP16) and WP16.	
Main tasks in the project: Leader: Task14.1; **WP16.0**; Task16.5 Contributor: Task13.1; Task13.3; Task14.2; Task16.1; Task20.3; Subtask20.3.6; Task25.1; Task25.3;	

21 -UM

Name of the legal entity	UNIVERSITEIT MAASTRICHT
Expertise, available infrastructure(s) UM, respectively, the department of bioinformatics and my main research interests are rare genetic diseases, especially neuronal and metabolic diseases, which I investigate using neuroscience, genetics, and bioinformatics methods. Within the EJP RD my WP13 (systems biology) investigated overlapping mechanisms - networks - between the disturbed metabolic and signalling pathways of the (rare) disease and environmental influences such as nutrition and toxicology - including building capacities and capturing knowledge in machine readable form in order to do this (= WikiPathways, rare disease community, my group is one of 2 major groups hosting and curating WikiPathways). I am an expert capturing biomedical knowledge and translate this in machine readable content for knowledge bases that can be used for data analysis - with or without using AI. Within the ERDERA DSH we build on these capacities, integrate new knowledge bases and use them for rare disease network construction in order to model concrete research questions, diagnosis, or treatment options.	
Main tasks in the project: Leader: **WP16.0**; Task16.4	

Contributor: Task16.5;

22 - EATRIS

Name of the legal entity	European Infrastructure for Translational Medicine ERIC
Expertise, available infrastructure(s) EATRIS, the European Infrastructure for Translational Research with over 150 top-tier academic centres across Europe, provides access to the entire pipeline of academic translational infrastructure and expertise, and optimises the route from discovery to proof-of-concept in medicines development. It provides a new development pathway, open to academic researchers and companies in need of support for advancing biomedical innovations. The EATRIS 'Coordination & Support' office employs 33 people, with expertise ranging from regulatory science, drug development and technology transfer to project management and science policy. EATRIS is a European Research Infrastructure Consortium (ERIC) since 2013, a legal entity established by the European Commission to facilitate the operation of international research infrastructures. Examples of EATRIS support and services - development planning: EATRIS matches clients' needs (ranging from biotech companies to academia and pharmaceutical industry) to the specific capabilities and expertise of the institutions, relying on a sophisticated and detailed database outlining EATRIS institutional capabilities, and based on the critical path needs of the project. Regulatory services include contact and filings with national competent authorities and EMA. - Industrial mentoring and feasibility assessment: EATRIS supports investigators and their funders in assessing the translational feasibility of their projects and portfolios, and provides access to industrial and other expert mentors for hands-on guidance.	
Main tasks in the project: Leader: **WP17.0**; Task17.1; **WP18.0**; Task 18.1; SubTask20.3.4; Task22.3 Contributor: Task17.2; Task20.3; WP22.0; Task22.1; Task22.2; Task22.4;	

23 - FGB

Name of the legal entity	FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS
Expertise, available infrastructure(s) FGB has 1) acted as a partner of EU and national projects to comply with the relevant requirements in clinical studies, consent and assent process, data collection and analysis, secondary use; 2) organised training activities at national and international level devoted to creating a critical mass of experts in the field of the regulatory sciences. FGB was also part of the study team of the Impact Assessment study on the revision of the Orphan and Paediatric Regulations contracted by the European Commission. FGB will lead/co-lead the ethics (Task 1.6) and regulatory (WP18) activities and mentoring and consultancy. Overall, the robust expertise in the regulatory and ethical field represents a key element to well-address these activities spanning from clinical and non-clinical studies and regulatory validation procedures to the collection of health data, guidance for researchers and protection of patient rights.	
Main tasks in the project: Leader: Task1.5; **WP17.0**; Task17.2; **WP18.0**; Task18.2 Contributor: Task5.1; Task5.2; Task5.3; Task14.1; Task17.1;	

24 - APHP

Name of the legal entity	ASSISTANCE PUBLIQUE HOPITAUX DE PARIS
Expertise, available infrastructure(s) AP-HP as a partner is made up of 5 ERN leaders who are also leaders of national rare disease networks where there are the largest number of patients with these pathologies in France. AP-HP is building up a network of hospital and university partners with clinical and research expertise, who already have lists of publications in prestigious journals, as well as national and European research projects. In these projects, the AP-HP can draw on the networked platforms of diagnostic excellence provided by the URCs and CICs, which specialize in clinical trials. The various AP-HP partners are part of the EJP-RD with leadership roles, and participate at national level in the BNDMR, AP-HP's own national structure. The culture of working with patient associations in a network and in collaboration with ORPHANET and INSERM.	
Main tasks in the project: Leader: Task9.2; **WP19.0**; Task19.1; Task19.2; Task19.3; Task19.4	

Contributor: Task6.2; Task6.3; Task7.4; Task9.1; Task9.3; Task10.1; Task10.2; Task10.3;

25 - UHASSELT

Name of the legal entity	UNIVERSITEIT HASSELT
Expertise, available infrastructure(s) Geert Molenberghs and the UHasselt/I-BioStat team has proven and long-standing expertise in basic and applied research and advanced education in biostatistics, with focus on clinical trials, longitudinal data, incomplete data, surrogate endpoints, and epidemiological methods. The team has strong expertise in computational aspects of both very small and very large studies. Geert Molenberghs was co-PI in EJP RD projects EBStatMax and iStore. He was an investigator within the IDEAL project, under the leadership of Ralf-Dieter Hilgers, and directed several researchers working on the project. The research in the above fields have led to numerous publications in the peer-reviewed literature. Geert Molenberghs is also (co-)author on several successful books on longitudinal data, missing data, surrogate endpoints in clinical trials, the estimation framework. He is currently co-editing a book on generalized pairwise comparisons.	
Main tasks in the project: Leader: **WP19.0**; Task19.2; Task19.3 Contributor: Task19.1; Task19.4; Task20.3; SubTask20.3.5;	

26 - EURORDIS

Name of the legal entity	EURORDIS - RARE DISEASES EUROPE
Expertise, available infrastructure(s) EURORDIS is a non-profit alliance of over 1000 RD patient organisations (from 74 countries) that work together to improve the lives of over 300 million people living with a rare disease. By connecting patients, families, and patient groups, as well as by mobilising the RD community, EURORDIS strengthens the patient voice and shapes research, policies, and patient services. Our mission is to work across borders and diseases to improve the lives of all persons living with a RD. This is done through the three-pronged strategy of: advocate, empower and partner. The contribution of EURORDIS has been key to the adoption of important rare disease and orphan medicine legislations at the European level, incl. the EU Regulation on Orphan Medicinal Products, the EU Regulation on Advanced Therapies, the EU Directive on Patients' Rights in Cross-border Healthcare. By partnering with RD National Alliances, EURORDIS also empowers national processes, and facilitates the adoption and implementation of national plans and strategies for rare diseases in European countries. EURORDIS will coordinate WP20 and will deliver an ambitious training programme for patients and young researchers. EURORDIS will also coordinate PPIE across the ERDERA and will contribute to different tasks bringing patients perspectives, preferences and expectations.	
Main tasks in the project: Leader: Task3.3; **WP20.0**; Task20.1; Subtask20.1.1; Contributor: Task1.2; Task2.2; Task2.3; Task3.1; Task5.1; Task5.3; Task7.1; Task7.4; Task10.1; Task10.2; Task10.3; Task11.1; Subtask20.1.2; Task20.2; SubTask20.3.7; SubTask20.4.1; SubTask20.4.2; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6; Task22.1; Task22.2; Task22.3; Task24.1; Task24.2; Task24.3; Task25.1;	

27 - VULSK

Name of the legal entity	VIESOJI ISTAIGA VILNIAUS UNIVERSITETO LIGONINE SANTAROS KLINIKOS
Expertise, available infrastructure(s) Vilnius University Hospital Santaros Klinikos is one of the largest University hospitals in Lithuania and Eastern Europe encompassing all main medical specialties. VULSK is founded by Vilnius University and Lithuanian Ministry of Health with three key assignments of highly specialized healthcare, research and education/training. Considerable part of VULSK human resources is active in research and education.	
Main tasks in the project: Leader: Task8.1; **WP20.0**; Task20.2; Subtask20.2.1; Task20.3; SubTask20.3.7; Task24.1 Contributor: Subtask20.2.2; Task20.4; SubTask20.4.1; SubTask20.4.2; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6; WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3; Task24.3;	

28 - UC

Name of the legal entity	UNIVERSIDADE DE COIMBRA

Expertise, available infrastructure(s)
The Group of Gene and Stem Cell Therapies for the Brain at University of Coimbra (UC) is devoted to the creation of effective therapies for brain diseases, as Machado-Joseph Disease, a rare neurodegenerative disorder, that can be moved from the bench to the bedside. For this, the group designs and uses technological platforms based on viral vectors, nucleic acids, exosomes and nanoparticles, gene editing, induced pluripotent stem cells, and neural Stem Cell and mesenchymal stromal cells. These technological platforms are the core of the Innovative Therapies Technology Accelerator WP of the WS Acceleration hub. UC is thus the academic lead of the Technology Acceleration WP and task leader of mRNA-based therapeutic strategies. The group has access to all the necessary infrastructure to carry out the project's activities, as molecular biology labs, cell culture rooms, animal facilities, a RI for viral vector production, experimentation and gene transfer, and a microscopy unit.

Main tasks in the project:
Leader: **WP21.0**; Task21.2
Contributor: Task21.1; Task21.3; Task21.4; Task21.5;

29 - FFRD

Name of the legal entity	FONDATION MALADIES RARES

Expertise, available infrastructure(s)
FFRD has a longstanding expertise in funding research through competitive calls, in the organization of scientific meetings, public-private partnerships, and open online trainings. FFRD has a strong track record of participation to international consortia (EJPRD, Simpathic RIA Horizon Health project, Erasmus+) and is a Member of the IRDiRC Funding Members Committee. Since 2019, it developed an intense activity of assistance to PAOs for the definition and management of their research efforts they dedicate to their specific disease.

Main tasks in the project:
Leader: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Task3.3; **WP22.0**; Task22.4; Task24.2; Task25.2; SubTask25.2.1; SubTask25.2.2; SubTask25.2.3
Contributor: Task1.3; Task2.3; Task5.1; Task5.3; Task20.2; Subtask20.2.1; Task22.1; Task22.2; Task22.3; Task25.1;

30 - AFM

Name of the legal entity	ASS FRANCAISE CONTRE LES MYOPATHIES

Expertise, available infrastructure(s)
AFM-Téléthon has been funding research project dedicated to rare diseases therapeutical development for more than 35 years. More particularly, it supported two laboratories dedicated to Gene therapy (Genethon) and Stem cells therapy (I-Stem) and a clinical centre dedicated to neuromuscular diseases (Institute of Myology) and clinical trials (I-Motion). Completing its experience in therapeutical development, AFM-Téléthon is also actively involved in several European research networks supporting Patient engagement in research (in the ERN EuroNMD and the European Joint Programme for Rare Diseases) and communication and collaboration between all pertinent stakeholders, clinicians, researchers, patients, pharmaceutical representatives and regulatory agencies representatives (ENMC). Finally, through its annual fundraising event, Téléthon, AFM-Téléthon has a long-term experience in communication to the global population around topics such as rare genetic diseases and innovative biotherapies.

Main tasks in the project:
Leader: Task22.2
Contributor: Task1.2; Task3.3; WP22.0; Task22.1; Task22.3; Task22.4;

31 - CCUH

Name of the legal entity	BERNU KLINISKA UNIVERSITATES SLIMNICA VALSTS SIA

Expertise, available infrastructure(s)
Madara Auzenbaha, MD, PhD, hold the position of Chief Physician for Rare Diseases at the Clinic of Medical Genetics and Prenatal Diagnostics. Alongside this, I am a PI at Riga Stradiņš University and an acknowledged

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expert by the Latvian Council of Science. I serve as the Chief Specialist in Rare Diseases at the Ministry of Health and am entrusted with the role of Orphanet National Coordinator. Additionally, I am an active member of the Board of Member States within the European Reference Networks. My responsibilities span projects funded by the Latvian Science Council, European Social Fund, and European Regional Development Fund, including initiatives like OD4RD II and JARDIN. With nearly 15 years of dedicated engagement in the field of rare diseases in Latvia, I possess understanding of the unique challenges faced by smaller countries operating within limited budgets. Over time, I have honed not only specific clinical knowledge but also valuable skills of communicating with patients and patient organisations. Within this project, my role encompasses co-leadership of WP 23 and Task 3 with UNEW. I will be instrumental in coordinating regular communication among various NMG, facilitating workshops, and contributing to annual meetings. Furthermore, I will participate in crafting best practice guidelines aimed at ensuring the sustainability of NMGs, as well as contributing to the preparation of peer-reviewed articles.
Main tasks in the project: Leader: **WP23.0**; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3 Contributor: Task8.4; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4;

32 - AICIB

Name of the legal entity	AICIB - AGENCIA DE INVESTIGACAO CLINICA E INOVACAO BIOMEDICA
Expertise, available infrastructure(s) The Agency for Clinical Research and Biomedical Innovation (AICIB) is an entity created by a Resolution of the Portuguese Council of Ministers, in 2018, to be the link between the Ministry of Health and the Ministry of Science and Technology. Its main mission is to promote, coordinate and support activities in the areas of clinical and translational research and biomedical innovation, contributing to the optimization of Portugal's clinical, scientific and technological potential. AICIB's mission is also to coordinate research to be priority-oriented based on several political instruments such as the National Health Plan, the Priority Health Programmes, the National Strategy for Personalized Medicine (PT_MedGen), or European Framework Programmes for R&D in Health. AICIB's internal structure is organized in "Pillars", one of which dedicated to the Internationalization of Research and Innovation in Health (International Pillar); participation in international initiatives is ensured within this Pillar (namely in what refers to the European Partnerships). Member of Portugal's National Mirror Groupe for Rare Diseases, with a professional team specialized in science, technology & innovation management, and in providing support, advice and assistance to the whole scientific and relevant business community (in the area of Health), and a record of active participation in more than a dozen Partnerships, AICIB has the appropriate institutional profile for assuming an active role in ERDERA, namely in the context of the Workstream "(Inter)national capacity alignment" and in the WP24 – Fostering the participation of Underrepresented Countries in ERDERA, specifically respecting the coordination of the joint efforts to be conducted for	**Expertise, available infrastructure(s)** The Agency for Clinical Research and Biomedical Innovation (AICIB) is an entity created by a Resolution of the Portuguese Council of Ministers, in 2018, to be the link between the Ministry of Health and the Ministry of Science and Technology. Its main mission is to promote, coordinate and support activities in the areas of clinical and translational research and biomedical innovation, contributing to the optimization of Portugal's clinical, scientific and technological potential. AICIB's mission is also to coordinate research to be priority-oriented based on several political instruments such as the National Health Plan, the Priority Health Programmes, the National Strategy for Personalized Medicine (PT_MedGen), or European Framework Programmes for R&D in Health. AICIB's internal structure is organized in "Pillars", one of which dedicated to the Internationalization of Research and Innovation in Health (International Pillar); participation in international initiatives is ensured within this Pillar (namely in what refers to the European Partnerships). Member of Portugal's National Mirror Groupe for Rare Diseases, with a professional team specialized in science, technology & innovation management, and in providing support, advice and assistance to the whole scientific and relevant business community (in the area of Health), and a record of active participation in more than a dozen Partnerships, AICIB has the appropriate institutional profile for assuming an active role in ERDERA, namely in the context of the Workstream "(Inter)national capacity alignment" and in the WP24 – Fostering the participation of Underrepresented Countries in ERDERA, specifically respecting the coordination of the joint efforts to be conducted for

addressing specific needs and expectations of Underrepresented Countries, foster collaboration, and boost inclusion of Underrepresented Countries (researchers and patient populations) in Rare Diseases R&I programmes.	addressing specific needs and expectations of Underrepresented Countries, foster collaboration, and boost inclusion of Underrepresented Countries (researchers and patient populations) in Rare Diseases R&I programmes.
Main tasks in the project: Leader: **WP24.0**; Task24.3 Contributor: Task25.1; Task25.3;	

33 - IMGGE

Name of the legal entity	INSTITUT ZA MOLEKULARNU GENETIKU I GENETICKO INZENJERSTVO
Expertise, available infrastructure(s) Prof. Maja Stojiljkovic, PhD (IMGGE) is a top grade researcher with 17 years of research expertise in the RD field and 12 years' experience in leading project/projects' WPs. She has 55 published papers (total IF 208.577, 900 citations, h-index 17) and 1 national patent. She is Coordinator of Serbian ORPHANET team, since 2022 (www.orpha.net), Secretary of ICORD, since 2019 (www.icord.es) and member of Expert Committee of National Organization for Rare Diseases of Serbia, since 2010 (www.norbs.rs). She was a member of the working group at the Ministry of Health Republic of Serbia that monitored and coordinated implementation of National program for rare diseases for 2020-2022. Prof. Stojiljkovic's role in the project is to identify actions to effectively increase participation of the UCs RD community in the partnership. Further-on she will work on proposing measures and guidelines aiming to increase UCs integration, and explore funding opportunities to leverage overall projects' budget.	
Main tasks in the project: Leader: **WP24.0**; Task24.3;	

34 - RDI

Name of the legal entity	Rare Diseases International
Expertise, available infrastructure(s) RDI is the global alliance of rare disease patient organisations across all countries and across all rare diseases. RDI's vision is a world where Persons Living with a Rare Disease (PLWRD) and their families experience a better life through full recognition and support. RDI's members include national and regional of RD patient organizations, and disease-specific international federations that, altogether, cover over 150 countries. RDI supports a Strategic Engagement Programme, providing PLWRD, patient representatives, and organisations a platform for learning, knowledge-sharing, and developing best practices. RDI is working to support healthcare systems strengthening through global networking of specialized expertise (Global Network of Rare Diseases); improve access to treatments and care for rare diseases through the essential model lists. RDI is well position to bring input from PLWRDs and lead the international dimension of ERDERA.	
Main tasks in the project: Leader: **WP25.0**; Task25.3 Contributor: Task1.2; Task10.3; Task25.1;	

35 - ACU

Name of the legal entity	ACIBADEM MEHMET ALI AYDINLAR UNIVERSITY
Expertise, available infrastructure(s) "Rare Diseases and Orphan Drugs Application and Research Centre-ACURARE", established in 2017 within Acıbadem Mehmet Ali Aydınlar University, aims to improve diagnosis and treatment opportunities in the field of rare diseases and orphan drugs. ACURARE employs expert clinicians, bioinformaticians, data analysts, genomic and molecular biologists, genomic scientists, and molecular biologists for the diagnosis, treatment research, and other translational medicine steps for undiagnosed and rare diseases. In this context, in ACURARE, we perform deep-phenotyping and/or re-evaluation of rare disease patients, DNA/RNA sequencing, variant analysis, advanced bioinformatic follow-up (if necessary), and functional analyses starting from the clinical step. Regarding infrastructure, ACURARE comprises a high-performance computer (Çirakoğlu-HPC), a research laboratory with facilities for genetics, molecular biology, cell biology, micro-imaging, and a research biobank.	

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Main tasks in the project: Leader: SubTask20.4.2; SubTask20.4.3 Contributor: Task20.4; SubTask20.4.1; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6;

36 - AIT

Name of the legal entity	AIT AUSTRIAN INSTITUTE OF TECHNOLOGY GMBH
Expertise, available infrastructure(s) The AIT is Austria's largest non-universitary research institutes. AIT's Digital Health Information Systems group has more than 20 years of experience in developing, deploying and maintaining IT infrastructures for clinical research, especially in the field of rare diseases, in telehealth solutions, and in privacy-preserving data services. The AIT is certified by ISO 9001 and ISO 13485. Within the EJP RD, AIT was responsible for the overall architecture of the EJP RD Virtual Platform. In the RD Partnership, the AIT will contribute to the evolution of the overall architecture of the developed IT solutions, privacy-preserving record linkage and services including their interoperability, semantic models and mapping services, and to the collection of ePREMs and ePROMs.	**Expertise, available infrastructure(s)** The AIT is Austria's largest non-universitary research institutes. AIT's Digital Health Information Systems group has more than 20 years of experience in developing, deploying and maintaining IT infrastructures for clinical research, especially in the field of rare diseases, in telehealth solutions, and in privacy-preserving data services. The AIT is certified by ISO 9001 and ISO 13485. Within the EJP RD, AIT was responsible for the overall architecture of the EJP RD Virtual Platform. In the RD Partnership, the AIT will contribute to the evolution of the overall architecture of the developed IT solutions, privacy-preserving record linkage and services including their interoperability, semantic models and mapping services, and to the collection of ePREMs and ePROMs.
Main tasks in the project: Leader: Task13.2 Contributor: Task14.2; Task15.1; Task15.3;	

37 - AMU

Name of the legal entity	UNIVERSITE D'AIX MARSEILLE
Expertise, available infrastructure(s) Computational and systems biologists, with expertise in developing methods and algorithms for data integration, with a special focus on approaches that can be applied to the study of rare genetic diseases. In the ERDERA, I will be involved in WP8: Genomic innovation to shorten time to diagnosis (and co-leading task 8.5) and WP16: Knowledge bases and ontologies for RD research. The partner Aix-Marseille Université (AMU) will receive the support of Protisvalor Mediterranée SAS (PVM), a spin-off company created by AMU to handle the financial and administrative aspects of AMU's projects. Protisvalor will act as In-kind contributors against payments of AMU. PVM is linked to AMU through a Framework Agreement validated by the French Ministry of Research and Higher Education (MESR), giving the right for PVM to administer. In H2020, PVM was involved in 116 projects whereas in HEUR PVM is involved until now in 53 projects. Consequently, PROTISVALOR will manage the administrative and financial aspects on behalf of AMU in the ERDERA project. The department will handle some means and expenses necessary for the fulfilment of the objectives of the project, e.g., purchasing necessary consumables and/or equipment; handling dissemination and publication costs; and any other necessary project expenses. All expenses incurred by PVM will be recorded in its own accounts and reported in the AMU financial report.	
Main tasks in the project: Leader: Task8.5; Contributor: Task16.4;	

38 – AOU MEYER IRCCS

Name of the legal entity	AZIENDA OSPEDALIERA UNIVERSITARIA MEYER IRCCS
Expertise, available infrastructure(s) The Neuroscience Department of the AOU MEYER IRCCS is an internationally renowned centre in the field of epilepsy and neurodevelopmental disorders. It includes two Paediatric Neurology and Psychiatry inpatient wards, Neurophysiology, Neurogenetics and Neurobiology Laboratories and a dedicated Neuropsychology team.	

The Department provides multidisciplinary care for children with neurological disorders, clinical and genetic studies of patients with epileptic encephalopathies and/or malformations of cortical development, neurophysiological studies, and presurgical evaluation and surgical treatment of children with epilepsy. The PI, Prof. Renzo Guerrini, is a world's leading expert in epilepsy genetics. He has coordinated 20 research Projects in Italy and in the UK (funding bodies: European Community, GKT Special Trustees, The Fund for Epilepsy, Telethon Foundation, Mariani Foundation, Italian Ministry of Health, Italian Ministry of Education, University and Research, Tuscany Region).
Main tasks in the project: Contributor: Task6.2; Task6.3;

39 – ASU-FC

Name of the legal entity	AZIENDA SANITARIA UNIVERSITARIA FRIULI CENTRALE
Expertise, available infrastructure(s) ASUFC MetabERN does coordinate the European Reference Network for Inherited Metabolic Diseases (IMDs). MetabERN groups 101 centres of excellence in 27 member states. Our vision is on establishing a growing and developing network to improve the lives of patients affected by rare IMDs. Our Mission is to identify and bring together the best expertise from across Europe to facilitate prevention, diagnosis, management, research and access to the best available care for metabolic patients. Our expertise relies on a) Pool knowledge and improve information exchange between members; b) Improve diagnosis and care c) in disease areas where expertise is rare; d) Support all Member States to provide highly specialised care to patients affected by IMDs; e) Advance innovation in medical science and health technologies for IMDs; f) Provide cross-border medical training and research on IMDs) Support all patient initiatives towards harmonising and improving all aspects of the care chain.	
Main tasks in the project: Leader: Task20.2; Subtask20.2.2; Task25.4 Contributor: Subtask20.2.1; Task25.1;	

40 - BIU

Name of the legal entity	BAR ILAN UNIVERSITY
Expertise, available infrastructure(s) Dr Hendel's lab aims to develop robust and safe CRISPR genome editing in primary cells to treat hematopoietic genetic disorders. Under Dr Porteus at Stanford University, Dr Hendel was the first to demonstrate improved CRISPR editing in human primary cells through chemically modified sgRNAs (PMID: 26121415, WO2016164356A1) with therapeutically relevant rates (PMID: 27820943, WO2017053729A1). Recently, the Hendel lab demonstrated successful CRISPR-Cas9/rAAV6 gene correction, generating T cells from RAG2-SCID patient-derived HSPCs (PMID: 36618262). The lab also focuses on developing protocols and standards to evaluate the specificity and toxicity of the editing process (PMID:32478125). These studies led to the development of CRISPECTOR, a software tool that supports the detection and quantification of editing activity from NGS data (PMID: 34031394, WO2021229569A1). Dr Hendel's expertise in detecting off-target events in edited HSPCs will be essential for the accomplishment of WP6.	
Main tasks in the project: Contributor: WP21.0; Task21.4;	

41 - BMBF

Name of the legal entity	BUNDESMINISTERIUM FUER BILDUNG UND FORSCHUNG
Expertise, available infrastructure(s) The German Federal Ministry of Education and Research (BMBF) supports innovative projects and ideas in research through targeted funding programmes. Funding is provided for projects in a wide spectrum of research areas, covering the whole range from basic research in natural sciences, environmentally friendly sustainable development, new technologies, information and communication technologies, the life sciences, work design as well as structural research funding at institutions of higher education to innovation support and technology transfer. BMBF has participated in various ERA-Nets such as ERA PerMed, E-Rare, ERA-CVD, InfectERA and TRANSCAN. BMBF is member of the IRDiRC innovation support and technology transfer.	

BMBF provides financial support to the Joint Transnational Calls (WP3). Within the programme, DLR and BMBF will act as an "institutional couple": Decisions on political, strategic and budgetary issues are taken by the BMBF and DLR-PT will speak and act according to these decisions.
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;

42 – CCRI GmbH

Name of the legal entity	ST. ANNA KINDERKREBSFORSCHUNG GMBH
Expertise, available infrastructure(s) The group of Prof. Boztug at CCRI GmbH has a long-standing expertise in diagnosing patients with inborn errors of immunity or haematopoiesis and the identification of novel causal variants in these disease entities via whole-exome sequencing. (e.g. PMID: 37342957, 37249233) The bioinformatics core unit of the CCRI GmbH maintains a powerful computational cluster and custom pipelines for the analysis of high-throughput multi-omics data. We will provide these resources and our experience to integrate the analysis of whole-exome sequencing data with bulk, as well as single-cell RNA-Sequencing data to identify novel disease-causing variants in patients with rare diseases. By implementing the analysis of single-cell data directly in the diagnostic pipeline we may uncover the underlying biology and specific cell types and aberrant developmental processes affected by genetic lesions in patients with unsolved rare disease and ultimately shorten the time to diagnosis of these patients. (PMID: 34826259)	
Main tasks in the project: Leader: Task8.4 Contributor: Task8.5; WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;	

43 - Centogene

Name of the legal entity	Centogene AG
Expertise, available infrastructure(s) Centogene has develop a diagnostic multiomic workflow to collect, store, analyse, interpret, and report molecular data using genome sequencing, whole blood transcriptomics, and targeted (and untargeted) metabolomics. Historic data from >700.000 patients has been collected and stored in the biodatabank where more than 400.000 cases have full research consent allowing the production of additional data and the use of such data in collaborative research. Within the research initiative (T7.3), we will further develop and scale up dried-bloodspot filtercard-based transcriptomics increasing yield and robustness of this medical device to help complementing diagnostics and monitoring of patients with rare molecular diseases. As a proof of concept, we could already show robust performance in hundreds of samples of observations studies (ROPAD and others) qualifying this sample collection method in analytical know how as an innovative diagnostic device overcoming typical limitations of current technology (especially regarding robustness, data quality, and comparability) in routine. Centogene has built up and grown an expert team for low-input diagnostics from global samples (see above) which high technical and medical expertise. All technical equipment for protocol optimization, product validation and IVD-registration, as well as a large European and global customer-base of physicians in need of accurate rare disease diagnostics is at hands.	
Main tasks in the project: Contributor: Task6.3; Task7.1; Task7.2; Task7.3;	

44 - CHARITE

Name of the legal entity	CHARITE - UNIVERSITAETSMEDIZIN BERLIN
Expertise, available infrastructure(s) The CHARITE team has well recognized expertise in i) biomarker development, qualification/validation, and application for in depth analyses of therapy response (core unit, spin-off company, biomarker monitoring of >100 clinical studies and >70,000 samples, >10 diagnostic products commercially available by diagnostics companies); ii) analysis and mitigation strategies of immunogenicity of gene and cell therapy products, iii) technology platforms for gene and base editing, RNA delivery for cell and gene products, iv) pipeline of novel	

cell and gene therapy products from preclinical to early clinical stage. Moreover, CHARITE team is experienced in leading national and international network projects, such as EU-funded consortia.
Main tasks in the project: Leader: Task21.5 Contributor: WP21.0; Task21.2; Task21.3;

45 - CHI

Name of the legal entity	CHECKIMMUNE GMBH
Expertise, available infrastructure(s) CHI is a spin-off company of CHARITE. The CHI team has a strong academic background with extensive experiences in basic and clinical immunological research. CHI is providing biomarker studies with focus on novel immunotherapeutics (small molecules, biologics, ATMP) and immunological challenges in other indication areas. With a track record of more than 50 industry-sponsored trials and 40,000 samples we acquired an excellent international reputation. CHI team has many years of experience in the preparation and implementation of biomarker analyses for (pre-) clinical studies, both industry-sponsored and investigator-initiated ones. CHI offers consultancy and laboratory services to support clinical development from preclinical studies to clinical trials, including the development, validation and application of immunological biomarkers for de-risking new drug developments and stratification of patient groups: i) drug candidate selection/validation, ii) therapy response monitoring (safety, efficacy), iii) mode-of-action, iv) surrogate markers, v) data interpretation (including medical advice). The laboratory has an accreditation according to DIN EN ISO 15189 and DIN EN ISO/IEC 17025, is EMA/FDA compatible and passed several audits successfully.	
Main tasks in the project: Contributor: WP21.0; Task21.5;	

46 – CHU DIJON

Name of the legal entity	CENTRE HOSPITALIER REG UNIVERSITAIRE DIJON
Expertise, available infrastructure(s) 10 years ago, our team was selected to lead TRANSLAD, a University Hospital Federation focused on the impact of the deployment of genomic medicine for patients with RD and their families. Since then, we have set up a number of genomic medicine pilot projects and an ES/GS offering in France. Many patients remain undiagnosed, and are keen to participate in research. On a national level, since 2013, Prof. Faivre have been tasked by the French Ministry of Health with the coordination the AnDDI-Rares health network. This network brings together 119 rare disease reference centres, 82 diagnostic labs and 32 research teams for developmental abnormalities. On a European level, Prof. Faivre lead the 'Training and Education' WG of the ITHACA ERN. The team also takes part in a number of international collaborations in the context of research projects, which led to the status as full partner in the European Solve-RD project. Since 2017, Prof. Thauvin led the France Genomic Medicine Plan in France.	
Main tasks in the project: Contributor: Task6.2; Task6.3; Task7.1; Task7.3;	

47 – Copenhagen Economics

Name of the legal entity	COPENHAGEN ECONOMICS AS
Expertise, available infrastructure(s) (1) Our Healthcare and Life Sciences team is recognised for its expertise within rare diseases and European regulation of orphan medicinal products (OMPs). We partnered with Hereditary Angioedema International (HAEi) and the European Haemophilia Consortium (EHC) to improve rare disease patient access to treatments. We're a knowledge partner for the European Expert Group on Orphan Drugs and have supported various companies in pharmaceutical lifecycle aspects. (2) Over the past several years we have helped research partnerships and grant giving organisations develop strategies and business plans to improve their organizations and maximize their commercial impacts. (3) We are one of the leading economics firms in Europe. We have repeatedly been placed among the global top 20 economics firms as rated by Global Competition Review, the leading independent ranker in the economics world. This reflects our high credibility in the eyes of important stakeholders and decision makers and reinforces the high impact of our work.	

Main tasks in the project: Leader: Task1.4;

48 – REGIONH (Copenhagen University Hospital)

Name of the legal entity	REGION HOVEDSTADEN
Expertise, available infrastructure(s) As a group we have more than 25 years' research experience in rare genetic disorders, which resulted among others, in identification of disease genes and establishment of genotype-phenotype correlations. We have a total of approximately 400 publications from our department during the last 5 years. We have all the necessary laboratory equipment for genetic and functional studies. We good possibility for patient recruitment via access to a vast array of rare disease patients and diagnoses in our national reference centre for rare diseases. We will contribute the project as research performers, and we will contribute to the testing/validation of approaches and ideas. We are deeply involved in education and training of health care providers in different aspects of genetics and metabolism, and will contribute to the project with our experience and knowledge. We have full access to the critical infrastructure of our department and hospital as employees of Capital Region of Denmark.	
Main tasks in the project: Contributor: Task6.2; Task6.3; Task7.2; Task8.5;	

49 – CSO-MOH

Name of the legal entity	MINISTRY OF HEALTH
Expertise, available infrastructure(s) The Ministry of Health bears national responsibility for ensuring the health of the population of Israel. The ministry determines the policy on matters of health and medical services, and is in charge of planning, supervision and control, licensing and coordination of the health system's services. CSO-MOH manages and funds health-related research and is responsible for the regulation of medical research in Israel. CSO-MOH takes part in 14 European networks and partnerships, including ERA4Health, THCS, TRANSCAN-3 and NEURON Cofund2. In ERDERA, CSO-MOH will provide financial support to the Joint Transnational Calls and will lead the tasks on monitoring of the JTC funded projects and the Networking Support Scheme events, as we have previously done in EJP RD.	
Main tasks in the project: Contributor: Task1.3; Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Task4.3; Task5.1; Task5.3;	

50 - CVBF

Name of the legal entity	CONSORZIO PER VALUTAZIONI BIOLOGICHE E FARMACOLOGICHE
Expertise, available infrastructure(s) Mentoring & consultancy: CVBF can provide expertise on regulatory issues covering requirements for the use of drug, diagnostics and devices in rare diseases. Methodological support - Clinical trial support & biostatistical support (beyond Clinical Trials): CVBF can provide Real World evidence/analysis e.g., epidemiological and pharmacoeconomic studies. Central Services: CVBF can support/perform the monitoring activities related to the ERDERA performance and impact. Specific expertise in ATMP. Support to the implementation of Clinical studies incl.: - Clinical trial design - Study start-up (including site selection) - Regulatory services (study authorization process in CTIS and at local level, informative material for patients, insurances and contracts with sites, including substantial amendments) - Clinical trial management (coordinating sites activation, eCRF training, central labs selection and management, IMP distribution to sites, biosamples management and clinical monitoring) - Data collection and statistical analysis, including plans and reports - Collection and reporting of adverse events, DSUR preparation and notification, SUSAR reporting trough EudraVigilance	

- Clinical Study Reports preparation, including lay summaries
Main tasks in the project: Leader: Task1.3 Contributor: Task10.3; Task11.1; Task11.4; Task24.1; Task24.3;

51 - DDF

Name of the legal entity	STICHTING DUCHENNE DATA FOUNDATION
Expertise, available infrastructure(s) "DDF is collaborating with GO-FAIR (https://www.go-fair.org/) for the FAIR treatment of Duchenne Data. DDF has prior expertise in statistical modelling, artificial intelligence and machine learning models. DDF has been also leading tasks related to ethical and legal issues (indicatively privacy, data protection, data governance, and ethical system design) by designing appropriate plans and strategies in full alignment of the EC Data Strategy objectives. Competences: 1.Use of data for the development of computational models for the disease and the in-silicon optimization of genetic therapies 2.Design and develop technical solutions for data storage and data preparation (modelling, integration, interoperability, etc.) 3.Provide data storage and publication for Duchenne data and metadata (Fair Data Point is deployed in the DDF repository) 4.Data and Knowledge management 5. Design, develop, and organize education and training activities on data ethics, FAIR data principles"	
Main tasks in the project: Leader: Task14.3 Contributor: Task9.6; Task13.2; Task20.1; Subtask20.1.1; Task20.3; Subtask20.3.6;	

52 - ELS

Name of the legal entity	ELSEVIER BV
Expertise, available infrastructure(s) Our solution is an affordable and reliable to way to 1) monitor research success, 2) showcase research findings and share with many audiences, and 3) create a database of experts in rare disease research. It is affordable as it uses off the shelve software used by hundreds of institutions in combination with innovative data management and a dedicated group of people minding your project. Whatever you and your researchers do well will be reported to and found by your key audience, whether they are financial backers, peers or patients. Our recent focus on rare disease research has enabled us to provide a layer of depth and analytics that will guarantee a very precise overview with many filters/ facets, such as persons, disease, institution, country, etc.	
Main tasks in the project: Contributor: Task1.3;	

53 – Erasmus MC

Name of the legal entity	ERASMUS UNIVERSITAIR MEDISCH CENTRUM ROTTERDAM
Expertise, available infrastructure(s) The Erasmus MC is home to one the largest rare disease programs in the Netherlands, and is member of several relevant ERNs (coordinator of ERN ERNICA and CRANIO (Craniofacial anomalies, are used as use case for PROM/COA development in the ERDERA WP 9. Task 9.1), active participant in ITHACA (incl. board memberships and WG leads). As an institution serving a population of > 1.5 million inhabitants in the South-West of the Netherlands in one of the most ethnically diverse cities in the country, we encounter the whole spectrum of rare diseases during the life course, from prenatal care to multiple paediatric care clinics in all relevant specialisms (amongst others within the expertise centre ENCORE and within the largest unit for critical ill children in the Netherlands), and towards unique clinics focusing on transition towards adulthood and adult care (incl. CRGS, the first multidisciplinary centre for adults with rare genetic syndromes worldwide, in the field of internal medicine). Our diagnostics and research laboratories are at the forefront of their fields, including access to routine diagnostics to diagnose unsolved patients using exome and whole genome sequencing (short read and long read), RNA-seq, routine metabolics and metabolomics. With many fundamental research groups	

within the Erasmus MC (incl. amongst others dept. of Cell Biology, Neuroscience, Molecular Genetics, Pathology), and multidisciplinary expertise groups we are uniquely positioned for innovative translational research benefitting unsolved patients in the context of ERDERA. Specific expertise and resources relevant for the proposal include well defined clinical rare disease cohorts and biological samples, and state-of-the-art genomics technologies including options to unravel the role of the non-coding genome in unsolved patients.
Main tasks in the project: Contributor: Task6.2; Task6.3; Task9.1; Task10.1; Task10.3;

54 – F.R.S.-FNRS

Name of the legal entity	FONDS DE LA RECHERCHE SCIENTIFIQUE- FNRS
Expertise, available infrastructure(s) The mission of the Scientific Research Fund - FNRS is to develop basic scientific research within the framework of initiatives presented by researchers. It promotes the production and development of knowledge by supporting, on the one hand, individual researchers and, on the other hand, by funding research programs, evaluated solely on a scientific excellence criterion, carried out in laboratories and services located mainly in the universities of the Wallonia-Brussels Federation. The F.R.S.-FNRS is also responsible for promoting European research and innovation programs in which the Wallonia-Brussels Federation participates to researchers, and supporting researchers for participation in these programs. The F.R.S.-FNRS has participated in several in multiple Horizon2020 ERA NETs (NEURON, EJP RD, etc.) and participates in several European partnerships (ERA4HEALTH, THCS, EP PerMed, ...)	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

55 - FHG

Name of the legal entity	FRAUNHOFER GESELLSCHAFT ZUR FORDERUNG DER ANGEWANDTEN FORSCHUNG EV
Expertise, available infrastructure(s) Fraunhofer has great expertise in the field of RNA-based therapeutics, mRNA formulation technology, and bioprocess development and GMP production of biomolecules as investigational drugs covering upstream (production) and downstream (purification) development, analytical method development and validation to formulation and sterile filling with subsequent stability testing and release for clinical trials. It is thus one of only a few non-industry locations that combines all the competencies required to transform a biopharmaceutical idea into an investigational drug for clinical trials. In the field of cell and gene therapy (ATMPs), Fraunhofer has become a leading institution in Europe. More than 500 products of the cell therapy drug Kymriah® (anti-CD19 CAR-T cells, Novartis) have already been manufactured as a contract. The scalable and robust technological platform for the development of mRNA therapeutics, AAV, and ATMPs can be provided as infrastructure to the ERDERA platform.	
Main tasks in the project: Contributor: Task11.3; WP21.0; Task21.1; Task21.2; Task21.3;	

56 - FRRB

Name of the legal entity	FONDAZIONE REGIONALE PER LA RICERCA BIOMEDICA
Expertise, available infrastructure(s) Fondazione Regionale per la Ricerca Biomedica (FRRB) is a private law institution established by Lombardy Region in October 2011. Its aim is to promote and enhance scientific research in the field of Life Sciences, particularly in the biomedical field. Having funded more than 100 research projects, both regionally and internationally, FRRB can ensure its support for boosting progress, research, development and innovation in hospitals, universities and research centres. In close collaboration with Lombardy region, the Italian region which invests the most in life sciences, the Foundation aims to invest local and European resources in innovative basic and translational research projects to generate positive impact on the local healthcare eco-system and citizens.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

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57 - ECRIN

Name of the legal entity	ECRIN EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

Expertise, available infrastructure(s)
ECRIN is a sustainable, not-for-profit, distributed infrastructure that provides support for the planning and implementation of multinational clinical research projects in Europe. ECRIN provides services for the management of multinational -investigators initiated and SME sponsored- trials; central services (data management through ECRIN certified data centres, central vigilance) and distributed services provided by the ECRIN partner in each country involved (regulatory and ethical submissions and follow-up, monitoring, local vigilance, project management etc.). ECRIN will participate in WP 17 and WP18 as consultant/mentor to support partners in clinical operations and in WP20 developing training to support the RD community interested in setting up multinational clinical trials in Europe

Main tasks in the project:
Leader: SubTask20.3.5
Contributor: Task20.3;

58 - FWF

Name of the legal entity	FONDS ZUR FÖRDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG

Expertise, available infrastructure(s) The Austrian Science Fund (FWF) is Austria's main funding organisation for basic research. The FWF supports the ongoing development of top-notch Austrian science and basic research based on international standards. One of the key objectives guiding the FWF's activities at the international level is to enhance Austria's international visibility as a research location. The FWF's international programmes include a variety of funding instruments which are essentially designed to support bilateral and multilateral research projects as well as international networking. The FWF will use its prior experience to make an active contribution to the activities related to the joint calls within the Partnership. The FWF's Department of Biology and Medicine has participated actively in many different ERA-Nets. The personnel involved have vast experience in running joint calls for projects, and in monitoring and strategic activities.	**Expertise, available infrastructure(s)** The Austrian Science Fund (FWF) is Austria's main funding organisation for basic research. The FWF supports the ongoing development of top-notch Austrian science and basic research based on international standards. One of the key objectives guiding the FWF's activities at the international level is to enhance Austria's international visibility as a research location. The FWF's international programmes include a variety of funding instruments which are essentially designed to support bilateral and multilateral research projects as well as international networking. The FWF will use its prior experience to make an active contribution to the activities related to the joint calls within the Partnership. The FWF's Department of Biology and Medicine has participated actively in many different ERA-Nets. The personnel involved have vast experience in running joint calls for projects, and in monitoring and strategic activities.

Main tasks in the project:
Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;

59 – IFD

Name of the legal entity	Innovation Fund Denmark

Expertise, available infrastructure(s)
Innovation Fund Denmark is a Danish public fund which participates in several European and Nordic collaborations mainly within the areas of health, digital technologies and green transition. As a research funder, IFD will be involved in the organisation of joint transnational calls for research projects, providing national funding for successful projects and supervision of project implementation.

Main tasks in the project:
Contributor : Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

60 – FSJD-CERCA

Name of the legal entity	FUNDACIO PRIVADA PER A LA RECERCA I LA DOCENCIA SANT JOAN DE DEU

Expertise, available infrastructure(s)

We have experience developing Antisensense Oligonucleotides Therapies and mRNA encoded CRISPR/Cas9: We have a design of gapmer antisense oligonucleotides to induce, via RNase H recruitment, the silencing of dominant alleles of collagen VI genes in primary fibroblasts from patients with muscular dystrophy. We have demonstrated the efficiency of a CRISPR/Cas9 gene editing for correcting dominant mutations in collagen VI genes (see López-Márquez et al., 2022 in publications). At present we are investigating in vitro and in vivo delivery systems for this strategy. Within the project we will participate in the WP21, "Technology Accelerator", where we will test the efficacy in vitro and in vivo and head-to-head comparison of conventional mRNAs, self-amplifying mRNA and circRNAs. The Institut de Recerca Sant Joan de Déu (IRSJD) is a research and innovation centre in biomedicine that offers specialised laboratories and equipment that allow our group to develop and test ATMPs for Rare Diseases.

Main tasks in the project:

FSJD-CERCA

Contributor: Task12.2; WP21.0; Task21.2; Task21.4; Task21.5;

61 - FCT

Name of the legal entity	FUNDACAO PARA A CIENCIA E A TECNOLOGIA

Expertise, available infrastructure(s)

FCT is the Portuguese national public agency that supports research in science, technology and innovation in all areas of knowledge, under responsibility of the Ministry of Science, Technology and Higher Education.
FCT pursues its mission through the attribution, in competitive calls with peer review, of fellowships, studentships and research contracts for scientists, research projects, competitive research centres and state-of-the-art infrastructures. FCT ensures Portugal's participation in international scientific organisations, fosters the participation of the scientific community in international projects and promotes knowledge transfer between R&D centres and industry. Working closely with international organisations, FCT ensure the technology and means for research, for science and for the development of new knowledge, serving a community of students, teachers and researchers, including through the development of national scientific computing resources.
FCT's role in the project is to act as funding organisation in the Joint Transnational Calls (WP3).

Main tasks in the project:

Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;

62 - MZd

Name of the legal entity	MINISTERSTVO ZDRAVOTNICTVI CESKE

Expertise, available infrastructure(s)

The Ministry of Health (MZd) is a central authority of the state administration for the health care, public health protection, health research activities, directly controlled health facilities, handling with drugs, preparations, and other agents, search, protection and use natural health resources, natural spas and mineral water resources, medicaments and technical equipment for prevention, diagnostics and treatment of people. Last but not least, MZd is responsible for health insurance and health information system.
The MZd as beneficiary will provide national funding for successful projects, sign contracts with successful Czech applicants and receive EC contribution.

Main tasks in the project:

Contributor : Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5

63 - GNT

Name of the legal entity	ASSOCIATION GENETHON

Expertise, available infrastructure(s)

Genethon is a not-for-profit organization, created in 1990 by the AFM-Telethon, an association of patients and patient families, thanks to the French Telethon.

Dedicated to the fight against rare diseases, Genethon has developed unique expertise in the design and development of gene therapy products, as well as their pre-clinical and clinical development. Its work is behind a number of treatments on the market, in clinical trial or at the R&D stage. Expertise on different aspects that are addressed in the project: AAV design, immuno-modulation, re-dosing, development of efficient and safe gene editing techniques to treat rare genetic diseases in vivo and ex vivo., AAV process development and manufacturing, quality standards as well as all regulatory aspects related to clinical development in rare diseases.
Main tasks in the project: Leader: Task11.2 Contributor: Task11.3; Task11.4; WP21.0; Task21.1; Task21.2; Task21.4;

64 - GERAD

Name of the legal entity	GEORGIAN FOUNDATION FOR GENETIC AND RARE DISEASES
Expertise, available infrastructure(s) As a representative of the GeRaD, leader organization in the field of rare diseases in Georgia, Oleg Kvlividze and his colleagues have experience and knowledge in 1. compiling data bases (information on research, clinical trials, patient organizations, medical professionals, patients registries, etc.); 2. conducting educational seminars/trainings for doctors, residents, students, nurses and patients on a wide range of the issues related to RD; 3. access to and fruitful communication with professional and patient communities; engagement of patients in research and clinical trials activities. GeRaD has created an Advisory Board, which includes the country's top specialists working on RD. The organization has staff (doctors, patients, lawyers, representatives of civil society) with strong experience in implementing various programs in the field of RD. As a result of the GeRaD collaboration with the School of Medicine, New Vision University, the Center on Rare Disease Research was founded, where several national research/projects on genetics and rare diseases are already underway.	
Main tasks in the project: Contributor: WP24.0; Task24.1;	

65 – RS (GMS-GMCK)

Name of the legal entity	REGION STOCKHOLM
Expertise, available infrastructure(s) We have for 10 years carried out large-scale sequencing of patients with rare inherited diseases. We have technical expertise relating to the molecular analyses, bioinformatic analysis and tools development, development of clinical decision support solutions as well as large-scale data structuring and management. We have access in-house to all key steps of the process, including sequencing, HPC for data processing and scalable data storage systems. We have a gender equality plan.	
Main tasks in the project: Contributor: Task6.2; Task6.3; Task7.3;	

66 - GUF

Name of the legal entity	JOHANN WOLFGANG GOETHE-UNIVERSITAET FRANKFURT AM MAIN
Expertise, available infrastructure(s) GUF is working in several large research networks and contributes its expertise in interoperability, federated analysis and software development expertise. Moreover GUF has relevant knowledge in the areas of clinical decision support, registry implementation and usability. Within EJP RD, GUF developed the domain specific common data elements to improve developing a core dataset as well as contributed largely to developing the VP-Portal.	
Main tasks in the project: Contributor: Task13.2;	

67 - HRB

Name of the legal entity	THE HEALTH RESEARCH BOARD
Expertise, available infrastructure(s) HRB is research funder. HRB was beneficiary and research funder within the European Joint Programme on Rare Diseases.	

HRB is also Involved as a research funder in the Genomics Data Infrastructure Project launched in November 2022. The project will make data accessible for research, clinical reference and policy development uses. HRB is involved in Pillar I on the legal framework and business models required to support European and national infrastructure operations. The organization will participate in the partnership as a funder in joint transnational calls.
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Task4.1; WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3; WP24.0; Task24.1; Task24.3;

68 - IBG

Name of the legal entity	IZMIR BIYOTIP VE GENOM MERKEZI
Expertise, available infrastructure(s) Izmir Biomedicine and Genome Center (IBG, www.ibg.edu.tr) is an advanced biomedical research and innovation centre with modern, state-of-the-art infrastructure and facilities, which are exceptional in Turkey in regard to quality, size and their unique composition. Furthermore, IBG is only CoE in the biomedical field making IBG the prime address for biomedical research in Turkey. IBG houses totally 30 basic and transnational research program, technological research program, industrial R&D program working on biomedicine and genome sciences. This multidisciplinary, cooperative nature is seen as a strong asset to address complex scientific questions. IBG will provide access to its state-of-the-art core facilities and services. In addition,4 technology platforms will be at disposal; IBG-BIP (Bioinformatics), IBG-Pharma (Biomedicine development), IBG-Nevcell (Steam cell and gene therapeutics) and IBG-Biobank (Biobanking facility and national node for the BBMRI-ERIC.IBG plans to spearhead and coordinate a national rare disease registry and repository including curated data and patient material.	
Main tasks in the project: Leader: Task20.4; SubTask20.4.6; Task24.2; Contributor: Task6.2; Task6.3; Task7.1; Task7.2; Task7.4; Task8.4; SubTask20.4.1; SubTask20.4.2; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3; Task24.1; Task25.1;	

69 - Rannis

Name of the legal entity	RANNSOKNAMIDSTOD ISLANDS
Expertise, available infrastructure(s) Rannis administers the main public competitive funds in the fields of research, innovation, education and culture in Iceland. Rannis coordinates and promotes Icelandic participation in European cooperation programmes, such as Horizon Europe, Erasmus+ and Creative Europe, as well as other international programmes.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

70 - IMAGINE

Name of the legal entity	IMAGINE INSTITUT DES MALADIES GENETIQUES NECKER ENFANTS MALADES FONDATION
Expertise, available infrastructure(s) Established in 2007 as a Scientific cooperation foundation, by the Assistance Publique-Hôpitaux de Paris (AP-HP), the French National Institute of Health and Medical Research (Inserm), the Université Paris Descartes, the French Muscular Dystrophy Association (Association française contre les myopathies (AFM), the Fondation Hôpitaux de Paris-Hôpitaux de France and the Mairie de Paris, the Imagine Institute of Genetic Diseases (http://www.institutimagine.org/en/) was accredited with Institut Hospitalo-Universitaire (IHU) status in 2011 and Institut Carnot status in 2019 under France's major Investment for the Future program. Its missions – patient-focused research, innovative care, education, training, and technology transfer – have the common goal of establishing better treatment and innovation in care pathway (“parcours patient”) for patients with genetic diseases. This project builds on a critical mass of experts – 1000 scientists, doctors, technicians, paramedical	

personnel, and therapeutic innovation professionals – established, all in one place in the Imagine building and the Necker-Enfants malades hospital campus, which takes care of patients and their families to provide them with the diagnostic and therapeutic solutions. 31 rare disease reference centres are affiliated to the institute. The institute has developed a strong expertise in genetic diagnostic, genome sequencing and analysis, rare variant analysis, gene editing, gene therapy, management of translational activity and development, management and consultancy in the RD research value chain, management of the innovation ecosystem. Imagine was involved in several training activities of the EJPRD programme and hosted the Eurordis Winter School for several years.
The institute will (1) Participate to the diagnostic research and genome analysis in WP7 Task 7.2: Standardised exome and genome re-analysis beyond state-of-the-art diagnostics), and in WP15 Task 15.3: Technical support for international genome-phenome federated analysis), (2) Participate to the execution of the mentoring programme (task 17.1) with the constitution of a database of multi-disciplinary experts, to patients and young researchers' training (task 20.1), (3) participate in the comparative evaluation of gene editing technologies and deliveries modalities in therapeutically relevant model systems of paradigmatic rare diseases (task 21.4) ACCESS. Numerous technical platforms are available at Imagine and Necker campus including genomics-sequencing, bioinformatics, mice/fish facilities, transgenic and knock-out mice facility, imaging (super resolution (STED) and TIRF microscopes), iPSC and Proteomics. All these platforms provide expertise and training (individual training or core courses).
Imagine will screen optimized gene editing and delivery reagents in human hematopoietic stem/progenitor cells (HSPCs) from patients with sickle cell disease (SCD), a disorder characterized by the abnormal production of haemoglobin that causes the formation of sickle-shaped red blood cells (RBCs). We will assess editing efficiency by next generation sequencing (NGS) and functional correction of erythroid cells by evaluating haemoglobin production ad by performing erythroid differentiation and sickling assay to estimate the frequency of abnormally shaped RBCs. The best-performing gene editing and delivery reagents will be tested in vivo to specifically target human HSPCs engrafted in immunodeficient mice. Editing efficiency and functional correction will be assessed in the progeny of long-term repopulating SCD HSPCs as described above for the in vitro experiments. The outcome of the study will be the development of a safe and efficacious therapeutic strategy for SCD.
The Clinical Bioinformatics Laboratory of the Institut Imagine, headed by Dr Antonio Rausell, develops statistical and machine-learning methods and bioinformatics pipelines for the computational assessment of human rare genetic variants in rare disease patients. Emphasis is dedicated to non-coding single nucleotide variants and structural variants with potential regulatory impact. The laboratory has recently developed a suite of machine learning and federated learning methods and best practices guidelines, mining clinical, genetic and multi-omics data. The Laboratory will contribute as a participant in WP7 Task 7.2: Standardised exome and genome re-analysis beyond state-of-the-art diagnostics, and in WP15 Task 15.3: Technical support for international genome-phenome federated analysis. Objectives will be the re-analysis of existing data through centralised and distributed approaches to discover novel genome-phenome associations in previously undiagnosed rare disease patients.

Main tasks in the project:
Contributor: Task7.2; Task7.3; Task15.3; Task20.1; Subtask20.1.2; WP21.0; Task21.4;

71 – IGC PAN

Name of the legal entity	INSTYTUT GENETYKI CZLOWIEKA POLSKIEJ AKADEMII NAUK

Expertise, available infrastructure(s)
The Institute of Human Genetics Polish Academy of Sciences (IHG PAS) is a key research centre in its field in Poland with broad scientific expertise in research on functions of the genome, transcriptome, epigenome as well as the molecular basis and epidemiology of genetic diseases. Research at the IHG PAS is aimed at elucidating the molecular basis of diseases, with particular emphasis on rare genetic diseases. Basic research carried out at the institute has both cognitive aspect, as well it can be applied in the diagnostics and treatment of diseases. The institute's role in the project is the provision of research and infrastructure, with the Innovative Medical Centre (IMC) or Laboratory for Advanced Tissue Models Imaging in place. The IMC uses the latest techniques such as DNA/RNA sequencing, spatial transcriptomics and single-cell analysis. The Centre is a certified provider of 10X Genomics Visium Spatial Gene Expression and a registered medical diagnostics laboratory

Main tasks in the project:
Contributor: Task6.2; Task6.3;

72 - ISCIII

Name of the legal entity	INSTITUTO DE SALUD CARLOS III

Expertise, available infrastructure(s)
ISCIII is the Public Research Organization of the Spanish Government responsible for funding and executing national biomedical research. It depends on the Ministry of Science, Innovation and Universities (MCIU), although it is also attached to the Ministry of Health, Consumption and Social Welfare (MSCBS). ISCIII created a specific centre for research on rare diseases (RD) in Spain, 2 decades ago, on the basis of long experience of its researchers, and the qualitative and quantitative importance of RD. It has participated in the different E-Rare initiatives and in the EJP RD (European Joint Programme on Rare Diseases), where ISCIII co-leaded 10% of its work packages and participated in 3 of 4 pillars. ISCIII is member of the Funders Constituent Committee of IRDiRC and is fully aligned with its 3 goals on diagnosis, therapies and their impact. ISCIII will participate in the ERDERA hosting one Joint Transnational Call secretariat, contributing to the definition of the call topics (co-leading task), leading a task in the Genomic research re-analysis pipeline, co-leading 2 subtasks on Education and research training, co-leading in the Public-private collaboration accelerator, and contributing to NMGs promotion and national alignment in Spain.

Main tasks in the project:
Team IIER
Leader: Task3.1; Task7.3; SubTask20.4.4; SubTask20.4.6; Task22.1
Contributor: Task1.3; Task3.3; Task6.1; Task7.1; Task7.4; Task9.1; Task20.4; SubTask20.4.1; SubTask20.4.2; SubTask20.4.3; SubTask20.4.5; Task22.3; WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.3; SubTask23.3.2; SubTask23.3.3; Task25.1;

Team SGPIRI
Leader: Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5
Contributor: Task3.1; WP23.0; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1;

73 - INSA

Name of the legal entity	INSTITUTO NACIONAL DE SAUDE DR. RICARDO JORGE

Expertise, available infrastructure(s)
INSA develops its activity as the Portuguese State Laboratory, National Reference Laboratory and National Observatory of the health sector. INSA collaborates with the ministry of health regarding legislation for rare diseases and genetics laboratories and it also actively collaborates in the national integrated strategy for rare diseases. INSA will coordinate the Portuguese National Mirror Group. INSA's Human Genetics Department has contributed for more than 3 decades now to the diagnosis and research of a large set of RD, including inherited metabolic diseases, thalassemia, haemophilia, among others. It is the major Portuguese centre in the diagnosis of RD (including the Portuguese Newborn Screening Program). A great effort has also been put in fostering the research activities involving all aspects of these pathologies and, as a consequence, INSA's team includes experts that have accumulated a large and very significant experience on RD that will be quite useful for RD partnership.

Main tasks in the project:
Contributor: WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;

74 - IOR

Name of the legal entity	ISTITUTO ORTOPEDICO RIZZOLI

Expertise, available infrastructure(s)
Strong track record of participation to international consortia (European Joint Programme on Rare Disease); Coordinator of ERN BOND; Competent Authority for Italy in the Joint Action for ERN Integration in the national healthcare systems JARDIN; Multiple years expertise in participation to Rare Diseases research projects consortia both as coordinator and participant; Organization of scientific meetings; Public-private partnership; education through the creation of multiple online open courses.

Main tasks in the project:
Contributor: Task25.4;

75 - ISS

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Name of the legal entity	ISTITUTO SUPERIORE DI SANITA

Expertise, available infrastructure(s)
ISS is the technical-scientific body of the National Health Service (NHS) and pursues the protection of public health, in particular through carrying out research, control, advisory, regulatory and training functions. ISS in the ERDERA will be involved in "Education and training activities in rare diseases research" (WP 20) and in "Data readiness services" (WP14). In both WPs ISS will organize or contribute to training activities mainly focused on FAIRification of Data and Data management on RD Registries.
ISS, in particular the involved staff, have extensive experience in RD registries, Bring Your Own Data on FAIR and training activities. In EJP RD, for example, ISS (Claudio Carta), coordinated the WP "training on data management and quality" and different tasks focused on organizing BYOD on "FAIRification of data at the source," and courses on rare disease data and registries.

Main tasks in the project:
Leader: Subtask20.3.6
Contributor: Task14.1; Task20.3; Task20.4; SubTask20.4.1; SubTask20.4.2; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6;

76 -IT-MOH

Name of the legal entity	MINISTERO DELLA SALUTE

Expertise, available infrastructure(s)
The Ministry of Health (IT-MoH) is the central body of the National Health Service and, as such, performs the functions belonging to the State regarding the protection of human health, the coordination of the National Health System. The Ministry of Health develops guidelines in the field of prevention, care and research in different health sectors and oversees National Health activities.
The Ministry of Health is the main public body funding biomedical research and biomedical innovation in Italy, while also overseeing research policy and stimulating the use of the generated knowledge in order to help improving the population well-being and the healthcare system in Italy. In particular, through yearly calls IT-MoH funds research for the improvement of the population's health through the rapid translation of research results into new or improved preventive, diagnostic, and treatment products and processes, and incorporation into health policies and practice.
At the international level, the Ministry of Health is involved in all EU Joint Actions accompanying measures (standardization, dissemination, policy, dialogues etc) and is also the governmental body of connection with the World Health Organization, the European Commission (health sector), the European Medicines Agency and OECD. IT-MoH is also involved in multiple European projects supporting research. In particular, as regards Horizon2020, it is involved in a wide range of ERA-NETs and CSAs (e.g. Euronanomed 2&3, ERACoSysMed, ERA-CVD, JPIAMR Action, ERA-PERMED and CSA on Personalised Medicine) and Joint Programming initiatives (JPND, JPI MYBL, EJP RD and JPIAMR). It is also committed to supporting EU projects for the development of the European Strategy Forum on Research Infrastructures (ESFRI) in the health research sector (ECRIN, EATRIS, BBMRI).
The Ministry of Health coordinates the EU Partnership on Transforming Health and Care Systems (THCS Partnership) under the Horizon Europe EU R&I framework programme, and takes part to other relevant Partnership under Horizon Europe (BeReady, EpPerMed, OHAMR, Era4Health)

Main tasks in the project:
Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Task4.3;

77 -KU Leuven

Name of the legal entity	KATHOLIEKE UNIVERSITEIT LEUVEN

Expertise, available infrastructure(s) Gert Matthijs is a molecular geneticist and head of the Laboratory for Molecular Diagnostics at the Center for Human Genetics at UZ Leuven. He is involved in the genetic diagnosis of congenital genetic diseases. He coordinates EuroGentest, a European network for the improvement and harmonization of genetic	**Expertise, available infrastructure(s)** Gert Matthijs is a molecular geneticist and head of the Laboratory for Molecular Diagnostics at the Center for Human Genetics at UZ Leuven. He is involved in the genetic diagnosis of congenital genetic diseases. He coordinates EuroGentest, a European network for the improvement and harmonization of genetic

diagnostics. The network focuses on the clinical, societal and ethical aspects of genetic research, and on the development of new technologies and new genetic tests. His scientific research focuses on 'Congenital Disorders of Glycosylation (CDG)', a group of rare inborn errors of metabolism caused by errors in the production of glycoproteins. His group is mainly engaged in a systematic search for new forms of these disorders and also tries to unravel the underlying pathophysiology through cell and animal models. In the context of applied research, the laboratory mainly focuses on the development and validation of new methods for genetic research based on next generation sequencing. Gert Matthijs has access to various large scale infrastructure (biobanks, omics platform, NGS platform) and is part of the University hospital.	diagnostics. The network focuses on the clinical, societal and ethical aspects of genetic research, and on the development of new technologies and new genetic tests. His scientific research focuses on 'Congenital Disorders of Glycosylation (CDG)', a group of rare inborn errors of metabolism caused by errors in the production of glycoproteins. His group is mainly engaged in a systematic search for new forms of these disorders and also tries to unravel the underlying pathophysiology through cell and animal models. In the context of applied research, the laboratory mainly focuses on the development and validation of new methods for genetic research based on next generation sequencing. Gert Matthijs has access to various large scale infrastructure (biobanks, omics platform, NGS platform) and is part of the University hospital.
Main tasks in the project: Leader: Task7.4; Task21.1 Contributor: Task6.2; Task6.3; WP21.0;	

78 - LZP

Name of the legal entity	LATVIJAS ZINATNES PADOME
Expertise, available infrastructure(s) LZP will be involved in organization of joint transnational calls for research projects, providing national funding for successful projects, supervision of project implementation	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

79 – MAPI Research Trust

Name of the legal entity	MAPI RESEARCH TRUST
Expertise, available infrastructure(s) Mapi Research Trust (MRT) is a non-profit organisation with a worldwide and sound PCOMs expertise. MRT has developed over the past 25 years a unique and comprehensive database of PCOMs, PROQOLID™, providing information on the conditions of use, translations, populations of intended use and development and validation process of 6000 PCOMs. PROQOLID™ is a hub for various RD databases: 1/ For each PCOMs described in ERICA RD PCOMS Repository, a link to PROQOLID™ is provided 2/ similarly, in Orphanet diseases database, for each RD with a PCOMs developed, a link to PROQOLID™ is reported. As a continuity of its work in ERICA project, MRT will provide their database expertise by continuing developing and expanding the functionalities of the RD-PCOMs repository in the ERDERA Virtual Platform (WP16.1). PCOMs and database expertise, as well as PCOMs unique database PROQOLID, makes MRT a key stakeholder in ERDERA in better assessing what matters for patients with RD.	
Main tasks in the project: Leader: Task16.1 Contributor: Task10.1;	

80 - MUS

Name of the legal entity	MEDICAL UNIVERSITY SOFIA
Expertise, available infrastructure(s) Molecular Medicine Center (MMC) is the main genomics research infrastructure of Medical University Sofia, Bulgaria. MMC offers biobanking, genetic, genomic services and has the capacity for WGS. Our biobank is the national hub of BBMRI-ERIC and hosts collections of samples and data from patients with rare diseases. We are partners in international consortia/networks (ICC, UDNI) and projects (GDI, EvolveBBMRI, JARDIN). The	

Genome Diagnostics Laboratory (GDL) at MMC has extensive expertise and offers CES, WES, microarray analysis, as well as other diagnostic tests. We provide efficient pre- and postnatal genetic diagnosis to patients with rare inherited disorders, and genetic counselling to their families. We will contribute data of the undiagnosed cases and our expertise to the Clinical Research network (CRN), WP6, WP7 (Data readiness and Genomic Research re-analysis pipeline) and the connected to them packages for Data Services Hub, as well as to the International capacity alignment WP.
Main tasks in the project: Contributor: Task6.2; Task6.3;

81 - MUH

Name of the legal entity	FAKULTNI NEMOCNICE V MOTOLE
Expertise, available infrastructure(s) Dept. of Biology and Medical Genetics (www.fnmotol.cz) is the largest academic medical/molecular genetics institution in Czechia and serves the National Coordination Centre for Rare Diseases (NKCVO) responsible for the implementation of a 10-year national strategy/action plans and having a state of the art genomics facility. NKCVO assured that Czechia is first within EU13 in terms of participation in the European Reference Network (ERN) for rare diseases (RD). NKCVO is chairing the national RD Task Force at the Min. Health and is a "clearing centre" for disseminating knowledge from various international projects on RD-related research/diagnostics (RD-connect.eu, Eurogentest.org, Solve-RD.eu) to the Central and Eastern European countries, including the Middle East. Prof. Macek is involved in the European Board of Member States for ERNs for RD, including the newly formed EU Advisory Board on ERN Sustainability, with a particular focus on underdeveloped regions in the EU, and beyond.	
Main tasks in the project: Leader: Task8.1 Contributor: Task6.2; Task6.3; WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;	

82 - MUR

Name of the legal entity	Ministero dell'università e della ricerca
Expertise, available infrastructure(s) MUR is the Italian ministry responsible for the definition of the National Research Programme, it manages most of the Public research programmes, Universities and many Research institutes. MUR is participating to the European Joint Programme on Rare Diseases; it has funded the first two calls. MUS has also participated to many Eranets cofund and it is participating in most of the new European partnerships. MUR is coordinating the Partnership on Sustainable Blue Economy; it provides the electronics submission platform for the partnerships Water4All and Clean Energy Transition. MUR is also managing the Call secretariat for Water4All.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

83 - NCBR

Name of the legal entity	NARODOWE CENTRUM BADAN I ROZWOJU
Expertise, available infrastructure(s) NCBR is a research funding agency. NCBR has participated as a funding agency in a wide variety of international research funding collaborations, including ERA-NET programmes from H2020 and before (ERA4Health, ERA PerMed, EuroNanoMed; Neuron Cofund, THCS). NCBR is part of the 1st joint call secretariat of THCS and is responsible for organisation of the call, in particular preparation of call documents, proposal assessment process or Peer Review Panel meeting in Warsaw. NCBR has extensive experience with joint-funded calls and management of research projects.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

84 - NKUA

Name of the legal entity	ETHNIKO KAI KAPODISTRIAKO PANEPISTIMIO ATHINON

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Expertise, available infrastructure(s) Our laboratory specializes in variant interpretation and genotype-phenotype correlation. Variant interpretation is not only limited to SNVs but also any kind of genetic variation, genetic or epigenetic. Our laboratory has several specialized departments and our members actively participate in ClinGen committees. Additionally, we have an outpatient clinic that sees patients with any type of genetic disorder and we function as the de facto genetic service of the biggest children hospitals in Greece providing the necessary clinical insight for the clinical validation of molecular findings. Our role in the project will be in data analysis and interpretation. Our scientific personnel have extensive expertise in variant analysis, pathogenicity estimation and designing specific strategies that lead to new gene discoveries. We have access to all the necessary infrastructure as we use it for our daily functions
Main tasks in the project: Contributor: Task6.2; Task6.3;

85 -MoH SR

Name of the legal entity	MINISTERSTVO ZDRAVOTNICTVA SLOVENSKEJ REPUBLIKY
Expertise, available infrastructure(s) Since 2011 SR has had an expert group at the MoH SR for rare diseases. However, this expert group is missing some representatives, such as the scientists. One of the advantages of the involvement of SR in this proposal will be to create and National mirror group in line with the European criteria, including all stakeholders. In the case of scientists' involvement, this could mean creating stronger interactions between healthcare and scientific research in rare diseases. Further advantages might be to support other activities and develop the National mirror group in line with the European requested criteria. Slovakia is still in most of the European projects an underrepresented country, thus it necessarily needs to create interconnections in all fields. On the other hand, the more than 10 years of experience of Slovak experts with rare diseases might be helpful and inspirative for other countries mainly in the promotion of National Mirror groups and national alignment. MoH supports ERN.	
Main tasks in the project: Contributor: Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;	

86 - RDG

Name of the legal entity	**Rare diseases Greece**
Expertise, available infrastructure(s) Rare Diseases Greece / RDG is a non-profit Association based in Athens covering the entire Greek territory, with 30 members non-profit organizations representing patients with rare diseases throughout the country. RDG is the largest organization of associations dealing with rare diseases in Greece, with representatives in Committees and Working Groups, such as the Committee for Rare Diseases, the Working Group for Rare Diseases for Rare Disease Patient Registry and Treatment Protocols, as well as the Pharmaceutical Expenditure Monitoring Committee of the Ministry of Health. RDG is the official representative body of Greece abroad, a member of the EURORDIS and the Council of National Associations of Europe through the Council of National Alliances. RDG will be responsible to build and manage the multistakeholder National Mirror Group (NMG), supporting in parallel the Communication, Dissemination and Engagement of the National stakeholder to secure the success of the project	
Main tasks in the project: Contributor: Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;	

87 – REGIONSYD

Name of the legal entity	Region Syddanmark
Expertise, available infrastructure(s)	

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Dept. of Clinical Genetics of Odense University Hospital is an accredited diagnostic centre with a genetic counselling clinic, a Center for Rare and Complex Diseases, and a fully equipped genetic lab. The project team of clinical experts and bioinformaticians are skilled researchers in rare disease genetics. Our approach involves genome sequencing of patients, cohorts, and advanced analysis techniques for novel diagnoses. We emphasize systematic reanalysis of existing data and exploring new genomics' potential. While primarily engaged in WP7, we also support WP6 and WP8.aWe have access to local and national critical infrastructure for specialized bioinformatics analysis and variant interpretation. Our local resources include the advanced Illumina DRAGEN on-premises server for genomic analysis, and we have direct access to the Danish National Genome Centre's HPC infrastructure and Variant Interpretations Platform, which houses advanced tools for efficient, high-quality interpretation of large scale genomic data. The Clinical Genetics Department of Vejle Hospital, an accredited diagnostic centre, features electronic patient records and laboratory information system. It houses a counselling clinic and a fully equipped molecular genetics laboratory staffed by experienced clinical and research professionals, including bioinformaticians. Our team specializes in rare diseases genetics. We aim to identify novel diagnoses by conducting genome sequencing on patients in our clinic, systematically gathering patient cohorts, and enhancing standard analyses with various complementary approaches. Our access to local and national critical infrastructure empowers us for advanced bioinformatics and precise clinical variant interpretation. We have direct access to the Danish National Genome Centre's HPC infrastructure and NGC Variant Interpretations Platform for detailed diagnostic interpretation of extensive genomic data.
Main tasks in the project: Contributor: Task6.2; Task6.3;

88 - OPBG

Name of the legal entity	OSPEDALE PEDIATRICO BAMBINO GESU
Expertise, available infrastructure(s) Marco Tartaglia is co-chair of the WG "Rare Diseases" of the EC's 1+MG Program (https://digital-strategy.ec.europa.eu/en/policies/1-million-genomes), and co-chair of the "research" WG of ERN-ITHACA (https://ern-ithaca.eu/) with the aim of facilitating collaborative research to understand rare genetic disorders, data- and knowledge sharing and establishing training programs. His research has been directed to elucidate the genomic bases of rare diseases, allowing the identification of more than 40 novel disease genes and a similar number of previously unclassified human diseases, including a newly described disorder with his name, Radio-Tartaglia syndrome (MIM: 619312). Besides gene identification interests are related to understanding the mechanisms of disease, and clinical variation and natural history of RDs. He has pioneered the genomics of "RASopathies". His track-record counts more than 400 publications, and his H-index is 63, with more than 17,000 citations, according to Scopus.	
Main tasks in the project: Contributor: Task6.2; Task6.3; Task8.5;	

89 - OSR

Name of the legal entity	OSPEDALE SAN RAFFAELE SRL
Expertise, available infrastructure(s) SR-TIGET is a world-recognized centre of excellence for research and clinical translation of Cell and Gene Therapy. The Institute is located within the OSR campus, which includes a large multi-disciplinary research hospital, a biomedical research centre, the Vita-Salute university and also hosts several biotechnologies companies. Over the years, SR-TIGET has given a pioneering and continued contribution to the gene and cell therapy field with relevant discoveries in vector design, gene transfer and gene editing strategies, stem cell biology, identity and mechanism of action of regulatory cells in immune responses and innate immune cells in cancer. SR-Tiget team, taking advantage of adequate institutional infrastructure and advanced technological facilities, will contribute to the partnership developing improved gene editing approaches towards therapy of rare diseases and will assess the therapy response of candidate technologies focusing on immune response.	
Main tasks in the project: Leader: Task21.4 Contributor: WP21.0; Task21.5;	

90 -JSI

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

Name of the legal entity	INSTITUT JOZEF STEFAN

Expertise, available infrastructure(s)
The leading Slovenian scientific research institute, covering a broad spectrum of basic and applied research. The staff specializes in natural sciences, life sciences and engineering. The mission is the accumulation and dissemination of knowledge at the frontiers of natural science and technology to the benefit of society at large through the pursuit of education, learning, research, and development of high technology at the highest international levels of excellence. Involved departments have expertise in different areas of artificial intelligence. The Centre for Knowledge Transfer in IT performs educational, promotional and infrastructural activities. The Centre is also the UNESCO Chair on Open Technologies for Open Educational Resources and Open Learning. Moreover, the International Research Centre on Artificial Intelligence (IRCAI) under the auspices of UNESCO is a coordination point, funding route and exploitation accelerator for approaches to the UN SDGs that make use of AI.

Main tasks in the project:
Contributor: Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;

91-RCN

Name of the legal entity	NORGES FORSKNINGSRAD

Expertise, available infrastructure(s)
The Research Council of Norway (RCN) is the national research strategy and research funding body. RCN distributes annually around 1 billion EUR for research purposes. RCN is the most important research policy adviser to the government, the ministries and other central institutions and environments with connection to research and innovation. RCN has a special responsibility for following up the government's long-term plan for research and to implement national research policy decisions through financing schemes. In collaboration with the research communities, the business community and the public sector, RCN works to give Norwegian research an economic and quality boost, and to promote innovation and knowledge. RCN works for greater international collaboration and increased participation in Horizon Europe. Other tasks include creating meeting places for researchers, trade and industry, public administration, public actors, and other users of research.

Main tasks in the project:
Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;

92 - FWO

Name of the legal entity	FONDS VOOR WETENSCHAPPELIJK ONDERZOEK-VLAANDEREN

Expertise, available infrastructure(s)
The Research Foundation - Flanders (FWO) is the funding agency that supports fundamental and strategic basic research at the universities and research centres of the Flemish Community, within Belgium. As a research funder, the FWO participation in the Rare Diseases partnership will be aimed at participating in joint transnational (co-funded) calls for research. The FWO participation remains mostly limited to the funding of its research community. No leading role in the partnership and its tasks is foreseen consequently.

Main tasks in the project:
Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;

93 - REUH

Name of the legal entity	RIGAS AUSTRUMU KLINISKA UNIVERSITATES SLIMNICA SIA

Expertise, available infrastructure(s)
The Riga East University Hospital (REUH) is one of the largest hospitals in the Baltic region, providing medical services, treatments, and specialized care. The hospital is affiliated with Riga Stradiņš University and University of Latvia. REUH has expertise in various medical fields, including rare diseases. Head of Rare disease centre is Dr Baiba Lace, clinical geneticist and a researcher known for her work in rare neuromuscular disorders, particularly focusing on their genetic and molecular aspects. The role of the current project is to identify problems related to under- representation of some of EU countries in the previous rare disease projects, and to develop instruments to overcome it in future. Additionally, REUH will be partner of rare disease clinical research network. REUH has necessary equipment, computing resources and facilities for the rare disease

research. In terms of the technical expertise, the team members are proficient in operating the infrastructure. It has collaborative partnerships with National and International Health institutes and Universities. REUH operates within legal and ethical frameworks and can offer support with project governance, financial planning and allocation of resources.
Main tasks in the project: Leader: Task24.1 Contributor: Task6.2; Task6.3;

94 - RIF

Name of the legal entity	IDRYMA EREVNAS KAI KAINOTOMIAS
Expertise, available infrastructure(s) RIF is the national agency responsible for promoting and supporting research, technological development and innovation in Cyprus. Part of its role is to coordinate the participation of Cyprus in European research and innovation activities, including the following: EU Framework Programmes, COST Programme, EURAXESS Network, EUREKA, Enterprise Europe Network (EEN), European Partnerships and Missions.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Task24.3;	

95 -RCSI Dublin

Name of the legal entity	ROYAL COLLEGE OF SURGEONS IN IRELAND
Expertise, available infrastructure(s) We have extensive expertise in the generation and analysis of genomic sequence data (DNA and RNA) in the context of rare disease risk factor identification and diagnosis. We have facilitated a positive molecular diagnosis in over 270 patients with rare disease (in Ireland). We have aided in the identification of multiple novel rare disease genes and risk factors (through NGS and GWAS studies). We have extensive experience of requirements gathering, deployment and testing of genomics-related software for clinical integration. We have designed and integrated one of the first genomics modules for an electronic health record system (to the best of our knowledge, the first for epilepsy).	
Main tasks in the project: Contributor: Task6.2; Task6.3;	

96 - RSU

Name of the legal entity	RIGAS STRADINA UNIVERSITATE
Expertise, available infrastructure(s) RSU is a university that uses a modern quality improvement approach ensuring high study and research quality, focused on continuous improvement and development. RSU is the leader in medical education and research in Latvia. The project will involve the Scientific Laboratory of Molecular Genetics which has expertise mainly with genetics of the RD, experience in innovation, and commercialization of innovation. RSU has all the necessary infrastructure to perform RD studies starting from the material collection, storage, isolation, analysis, and bioinformatic analysis that is performed in strong collaboration with the Rare Neurological Disease Center at P. Stradins University Hospital and other clinical units and specialists in Latvia working in RD field. RSU will participate with the contribution of data in unsolved cases, will take part in creating a European curriculum in RD research, and will contribute to unlocking the underrepresented countries' potential in RD research.	
Main tasks in the project: Contributor: Task20.4; SubTask20.4.1; SubTask20.4.2; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6; Task24.2;	

97 - SCIENSANO

Name of the legal entity	SCIENSANO
Expertise, available infrastructure(s) SCIENSANO will be participating in WP9 - Real World Data and more specific Task2.9: Use of population-based data for RD outcome research. We already have the necessary expertise and data capture infrastructure in our institute; hence, we were contacted by BE HCP to create the Belgian Registry for Hirschsprung's disease	

conform with the initiatives that are undertaken on the ERN ERNICA level. Subsequently, we would like to link patient data (demographics, symptoms, diagnostics, surgical therapy and long-term follow-up until adolescence, ...) with a PROM validated questionnaire filled out by patients/carers to ensure long-term follow-up on QoL aspects. In order to improve data quality and completeness, a Source Data Verification link will also be provided to the IMA/AIM (InterMutualistisch Agentschap/Agence InterMutualiste) which is the BE Institute collecting detailed data on healthcare and drug reimbursement by 7 BE mutual insurance companies. Data elements to be collected from IMA/AIM include: (1) information on additional surgeries; (2) readmissions linked to abdominal problems; (3) identification of contacts of patients with other healthcare professionals such as physiotherapist, ...; (4) information on treatments / drugs provided to the patients. Sciensano will be responsible for the creation of the registry, data capture, validation, analyses and linkage to the IMA database. SCIENSANO is also leading Task 10.3 on the quantification of the socioeconomic impact of rare disease, based on our experience in burden of disease assessment
Main tasks in the project: Leader: Task10.3 Contributor: Task9.2;

98 - SPW

Name of the legal entity	SERVICE PUBLIC DE WALLONIE
Expertise, available infrastructure(s) The Service Public de Wallonie (Belgium) is a public agency. The Research Programs Direction coordinates, develops and manages regional, federal and international research programs. It evaluates, finances and monitors research projects introduced by universities, high schools, approved research centres or Walloon companies, and submits notices of opportunity, while evaluating the impact of these projects. Our role in ERDERA is thus the funding of research projects.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

99 - SFU

Name of the legal entity	SIGMUND FREUD PRIVATUNIVERSITAT WIEN GMBH
Expertise, available infrastructure(s) Prof. Dr rer. medic. Nicole Heussen is biostatistician. Her methodological research interest centres around the design of clinical studies and randomization based inference. Both topics are highly relevant for planning, conduct and analysis of rare disease clinical trials. Beyond that, she is challenged by explaining complex statistical issues to non-statisticians. She provides consultation for clinical and pre-clinical studies in various medical disciplines. Moreover, she teaches medical students as well as students from other bio-scientific areas. She will contribute to the project via WP19 in transferring biostatistical knowledge towards local clinical trial teams and WP20 in providing trainings on biostatistical topics to empower RD clinical trial methodologies and management.	
Main tasks in the project: Leader: Task19.1; SubTask20.4.2 Contributor: Task20.3; SubTask20.3.5; Task20.4; SubTask20.4.1; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6;	

100 - ETAg

Name of the legal entity	SIHTASUTUS EESTI TEADUSAGENTUUR	
Expertise, available infrastructure(s) ETAG (Estonian Research Council) has participated as Task Leader and supporter in many Horizon 2020 ERA-NETs (e.g. SusCrop, BlueBio, CoBioTech etc.) and Horizon Europe partnerships (e.g. Biodiversa+, Water4All, Sustainable Blue Economy etc.). Additionally, ETAG has participated as a secretariat for ERA-NET CHANCE and Biodiversa and provided the submission platform for different ERA-	**Expertise, available infrastructure(s)** ETAG (Estonian Research Council) has participated as Task Leader and supporter in many Horizon 2020 ERA-NETs (e.g. SusCrop, BlueBio, CoBioTech etc.) and Horizon Europe partnerships (e.g. Biodiversa+, Water4All, Sustainable Blue Economy etc.). Additionally, ETAG has participated as a secretariat for ERA-NET CHANCE and Biodiversa and provided the submission platform for different ERA-NETs and	

NETs and partnerships (e.g. Biodiversa and Biodiversa+, CHANCE, Sustainable Blue Economy, etc.). ETAG is also one of the main funding organisations for Estonia.	partnerships (e.g. Biodiversa and Biodiversa+, CHANCE, Sustainable Blue Economy etc.). ETAG is also one of the main funding organisations for Estonia.
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

101 - SAS

Name of the legal entity	SLOVENSKA AKADEMIA VIED
Expertise, available infrastructure(s) SAS is a research funding agency. SAS has participated as a funding agency in previous international research funding collaborations, including EJP RD. SAS has extensive experience with joint-funded calls and management of research projects.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

102 - SONIO

Name of the legal entity	SONIO
Expertise, available infrastructure(s) At Sonio our expertise is multidisciplinary, both in AI, bioinformatic, genetic and clinical prenatal diagnosis (maternal foetal medicine practitioners - MFM). Our role will be to provide to Orphanet the work we have done of curation of rare disease phenotype for the antenatal onset. We will take this opportunity to improve further this database with new curations taking advantage of the network of clinician experts we built over the last years and rely on our bioinformatic expertise. In a second time our objective is to determine with Orphanet a second list of syndrome which has not a prenatal phenotype sufficiently specific to diagnosed by MFM but that could be diagnosed by combining antenatal phenotype and genotype. Here we aim to go further in the curation work initiated during our EIC project.	
Main tasks in the project: Leader: Task16.2;	

103 - MOSAE

Name of the legal entity	SOTSIAALMINISTEERIUM
Expertise, available infrastructure(s) MOSAE has participated as a funding agency in international research funding collaborations. The organization will participate in the partnership as a funder in joint transnational calls.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

104 - SRC

Name of the legal entity	VETENSKAPSRADET - SWEDISH RESEARCH COUNCIL
Expertise, available infrastructure(s) The Swedish Research Council (SRC) is the largest governmental funding agency in Sweden. We operate under the Ministry of Education and Research and fund research and research infrastructure in all scientific disciplines with an annual budget of around 8 billion SEK.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

105 - TEDDY

Name of the legal entity	TEDDY - EUROPEAN NETWORK OF EXCELLENCE FOR PAEDIATRIC CLINICAL RESEARCH
Expertise, available infrastructure(s) TEDDY is willing to participate to the project due to its consolidate expertise in the field of medicines and innovative treatment for special population ed in particular of medicines for children affected by rare diseases. TEDDY started as an EU FP6 funded project, ended with methodological, ethical and regulatory experts	

recommendation, and is currently a member of the coordinating group at the EnprEMA. TEDDY will contribute to the following project activities: a)organise knowledge exchange meetings and peer education activities addressing ethical, legal, and social aspects of paediatric research and children rights. b) Setting up, managing, and implementing rare disease (RD) Paediatric Advocacy groups covering local, regional areas and underrepresented EU countries. c) providing Ethical and Regulatory support including involvement of children and young patients groups in trial design and studies conduct. d) supporting methodological expertise in developing paediatric research protocols and RWD collection.
Main tasks in the project: Leader: Subtask20.1.2 Contributor: Task2.3; Task18.2; Task20.1;

106 - TEKKARE

Name of the legal entity	Real Consulting Data
Expertise, available infrastructure(s) Tekkare has a strong expertise in user experience, software development and data engineering. This ability to deliver efficient solution based on reliable data processing showcase with its nomination for prix Galien 2023 as category best digital product for its rare disease medical device for HCP. Tekkare has also contributed to many scientific studies in rare diseases as a technical support. Tekkare is bringing proven software and capabilities that will help strongly accelerate the data effort for monitoring, analysis and development of a knowledge hub to improve user experience and exploration of the data generated by the consortium.	
Main tasks in the project: Leader: Task1.3 Contributor: WP1.0;	

107 - TIF

Name of the legal entity	THALASSAEMIA INTERNATIONAL FEDERATION
Expertise, available infrastructure(s) The Thalassaemia International Federation (TIF) is a Cyprus-based, WHO-awarded, patient-oriented, non-profit, non-governmental federation with 134 members (national thalassaemia associations) in 68 countries globally (incl. 26 in 16 EU MS). TIF focuses on the disease-specific education of patients and healthcare professionals, the promotion of research on haemoglobinopathies, advocacy for health/social policy/service improvement, awareness-raising and networking. With a renowned educational programme, well-established networks of expert patients, researchers/healthcare professionals, and meaningful collaboration with the rare disease community in Cyprus and globally, TIF may substantially contribute to attaining ERDERA's objectives.	
Main tasks in the project: Contributor: WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;	

108 - TUBITAK

Name of the legal entity	TURKIYE BILIMSEL VE TEKNOLOJIK ARASTIRMA KURUMU
Expertise, available infrastructure(s) TÜBİTAK is participating as a funding agency in 7 different HE partnerships. As for H2020, TÜBİTAK has been a partner for 510 different ERA-NET Cofund projects and 1 COFUND-EJP project. Thus, TÜBİTAK has significant expertise on how to manage external calls and their related actions.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Task24.3;	

109 – RT (TuscReg)

Name of the legal entity	REGIONE TOSCANA
Expertise, available infrastructure(s) The Tuscan health system includes three Local Health Authorities, four university hospitals, ISPRO Institute and Monasterio Foundation. The health system is the sector to which the region commits the largest share of its budget and organizational structure, and constitutes an infrastructure of services and activities that can generate	

positive effects throughout the region Tuscany Region promotes health research and innovation policies to structure an integrated and synergistic research and innovation system in a coordinated context among Tuscan university hospitals and other institutions of the Regional Health Service. The Rare Diseases Regional Network, recently implemented close to the ERN model, includes institutions, clinicians, researcher and patients. The Region is also actively involved in the promotion of the Tuscan Life Sciences Cluster for a dialogue among companies and the network of excellence present in the field of research and technology transfer in the region.
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Task3.3;

110 - UAB

Name of the legal entity	UNIVERSITAT AUTONOMA DE BARCELONA
Expertise, available infrastructure(s) CBATEG is a translation gene therapy research centre focusing on the development of AAV vector-based gene therapy approaches for both rare and highly prevalent metabolic and neurodegenerative diseases. CBATEG has been working in all aspects of gene therapy development for over 20 years, including the development and preclinical validation of AAV-based ATMPs, and the rational design and generation of tailored and optimized AAV-based expression cassettes and pre-clinical AAV manufacturing. We have also an extensive experience in AAV vector characterization and assessment of quality attributes, using different state-of-the-art techniques that meet the regulatory EMA and FDA requirements. CBATEG has AAV vector preclinical production laboratories equipped to produce high quality AAV vectors and laboratories for process development for the manufacturing of AAV, including bioreactor production and purification equipment. We will contribute to improve manufacturing processes, develop analytical methods and assays to better characterize new medicinal products, and address evaluation of therapy response as well as immunogenicity issues related to in vivo administration of ATMPs.	
Main tasks in the project: Contributor: WP21.0; Task21.1; Task21.4; Task21.5;	

111 –UCD

Name of the legal entity	UNIVERSITY COLLEGE DUBLIN, NATIONAL UNIVERSITY OF IRELAND, DUBLIN
Expertise, available infrastructure(s) UCD team consists of experienced researchers from early careers to experienced health and social care researchers, including nursing, health systems and global health and policy. Our current role in the EURD project is to co-lead Task 20.4: European Diploma on RD research (M1-M84) The UCD (Dr Somanadhan) will lead a module co-design, development and delivery as part of the European Diploma on RD research. Also, Co-lead (Dr Somanadhan) for Subtask 20.4.1: Establish a cross-ERDERA expert consortium and set of training modules (M1-M12)	
Main tasks in the project: Leader: SubTask20.4.1 Contributor: Task20.4; SubTask20.4.2; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6;	

112 - UCSC

Name of the legal entity	UNIVERSITA CATTOLICA DEL SACRO CUORE
Expertise, available infrastructure(s) UCSC comprises 4 campuses (Milano, Brescia, Piacenza-Cremona, Roma) and 12 faculties covering several disciplines, from economics and humanities to biomedical sciences and STEM. The Faculty of Medicine and Surgery, in the Rome Campus, collaborates with its teaching hospital, Fondazione Policlinico Universitario Agostino Gemelli (10% of the entire productive capacity of Lazio Regional Health Service with almost 100’000 patients cared every year and involved in 16 ERNs, and housing an up-to-date research facilities at the Gemelli Science and Technology Park https://gstep.policlinicogemelli.it/). It runs >100 academic curricula (master’s and bachelor’s degrees, advanced courses, PhD programs, residency schools, etc), houses fully teaching facilities	

(fully equipped for videoconferencing, teaching labs, lab simulations software and immersive learning tools). The School of Medicine is at present a world-class training ground for future leaders in medical research and practice -including every modern medical discipline and some of the most respected medical scholars in the world. UCSC will be mostly involved in setting up and running the academic curriculum on RD research within the training activities, and will collaborate with expert mentoring in data processing from clinical research tasks.
Main tasks in the project: Leader: Task20.4; SubTask20.4.4; SubTask20.4.5 Contributor: Task20.2; SubTask20.4.1; SubTask20.4.2; SubTask20.4.3; SubTask20.4.6;

113 - UEF

Name of the legal entity	ITA-SUOMEN YLIOPISTO
Expertise, available infrastructure(s) The University of Eastern Finland responds to global challenges through a high standard of interdisciplinary research and education. In doing so, we build a responsible and sustainable future. Our strategic research is focused on four profile areas: Ageing, lifestyles and health ; Environmental change and sustainable use of natural resources ; Cultural encounters, mobilities and borders ; Diversifying learning and interaction.	
Main tasks in the project: Contributor: WP21.0; Task21.2; Task21.3;	

114 - UKA

Name of the legal entity	UNIVERSITAETSKLINIKUM AACHEN
Expertise, available infrastructure(s) Prof. Dr rer. nat. Ralf-Dieter Hilgers is mathematician by training. His research interest is in optimal design of experiments, randomizations process and clinical trials. He gives biostatistical advice to clinical and experimental trials in all medical areas. He teaches students in different bio-scientific areas and is responsible for the education of investigators in clinical trials. He also acts as reviewer for methodological and clinical journals. He coordinates the FP-7 funded IDeAl project (GA N° 602552) (www.ideal.rwth-aachen.de), co-leads WP20 “Accelerating the validation, use and development of innovative methodologies tailored for clinical trials in RDs“ within H2020 funded EJP-RD (GA N° 825575) and co-leads of WP4 Clinical Trial Support with ERICA (GA N° 964908). He is reviewer for professional societies and member of the Off-Label Expert Group and Commission C of the BfArM. He will contribute to WP20 with teaching in biostatistics and WP19 - Task 19.4.	
Main tasks in the project: Leader: Task19.4; SubTask20.4.1 Contributor: Task19.1; SubTask20.3.5; SubTask20.4.2; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6;	

115 - UKLFR

Name of the legal entity	UNIVERSITAETSKLINIKUM FREIBURG
Expertise, available infrastructure(s) • Prof Kirschner has extensive experience in clinical research for neuromuscular and other rare diseases. His main focus is the development of innovative treatments (including ATMP) and the collection or real-world data. • Prof Cathomen leads the analyses of off-target effects of cells edited ex vivo and organs edited in vivo. • Dr Mussolino contributes to the efforts of developing and applying novel Cas fusion proteins that promote HDR and reduce mutagenic outcomes. • Dr Pechmann is lead investigator of the SMArtCARE database to collect real-world data from patients with spinal muscular atrophy. • Dr Rodger curates the Care and Trial Site Registry, and contributes user-centred design expertise to technology and service development.	
Main tasks in the project: Contributor: Task9.5; Task12.3; Task13.2; WP21.0; Task21.4;	

116 – University of Campania L.

Name of the legal entity	UNIVERSITA DEGLI STUDI DELLA CAMPANIA LUIGI VANVITELLI

Expertise, available infrastructure(s)
V. Nigro is the Coordinator of the Telethon Program on Undiagnosed Diseases and Director of the Medical Genetics Service at Vanvitelli University. In the last 10 years, more than 10,000 Italian patients have been studied at least by exome sequencing and a 1.2k paediatric cohort of undiagnosed cases have been fully characterized both genomically and phenotypically in the Telethon program. The Nigro team at Vanvitelli now consists of 46 people, including 18 permanent staff, including medical geneticists, bioinformaticians, technicians, administrative staff, a cardiologist, and the facility is equipped with several sequencers, including Illumina NovaSeq6000, Next 500, Oxford Nanopore Promethion 24 and Bionano. Recent focus is on the use of beyond exome technologies, including methylome and transcriptome analysis. One of the in-house technology enhancements is aimed at the detection of copy number elusive variants (CNVs), such as ACACIA, a custom megabase array CGH that allows the assessment of the copy number of predicted haplo-insufficient genes at single exon resolution. Vanvitelli is a founding member of the Network for Italian Genomes (NIG), UDNI, and a beneficiary of SOLVE-RD.

Main tasks in the project:
Contributor: Task6.2; Task6.3;

117 – University of Crete

Name of the legal entity	PANEPISTIMIO KRITIS

Expertise, available infrastructure(s)
The focus of Ioannis Zaganas research is on the genetic basis of rare neurogenetic disorders, including myopathies, polyneuropathies, epilepsies, motor neuron disorders, ataxias etc. He is also interested in the genetic underpinnings and the molecular mechanisms of neurodegeneration, especially in relation to Alzheimer's disease, Frontotemporal Dementias and other dementias. Through his laboratory (Neurology/Neurogenetics Laboratory, University of Crete), more than 1,000 genetic tests have been performed, including more than 600 whole exome sequencing analyses, most of them for rare neurogenetic disorders. Most of these analyses have been contributed to the SOLVE-RD consortium and are currently under re-analysis. His aim in the current proposal is to contribute genetic sample data of unsolved cases and assist in interpretation of these and other datasets. Hopefully, following identification of causative variants in this project, he will communicate these results to patients and/or attending physicians.

Main tasks in the project:
Contributor: Task6.2; Task6.3;

118 - UGENT

Name of the legal entity	UNIVERSITEIT GENT

Expertise, available infrastructure(s)
UZ Gent is one of the seven Belgian University Hospitals that received recognition as a 'Rare Disease Function', an access point to interdisciplinary diagnosis, treatment and follow-up for patients with an undiagnosed disease. At the local level, UGent/UZ Gent has developed clinical and research-oriented rare disease initiatives such as UD-PrOZA and RARE-MED. Internationally, UGent/UZ Gent belongs to 21 ERNs, UDNI and Solve-RD. In the present proposal UGent/UZ Gent will contribute to the Genome Research Re-analysis Pipeline Work package by (1) contributing thousands of omics datasets (exomes, genomes, transcriptomes) of unsolved disease cases generated as part of the genetic diagnostic work-up on state-of-the-art genomics platforms (Illumina Novaseq 6000) and (2) taking a leading role in the data interpretation task force for neurological (neuromuscular/neurodegenerative) disorders including functional validation to prove pathogenicity of variants for known and novel disease-genes.

Main tasks in the project:
Contributor: Task6.2; Task6.3; Task7.1; Task7.3;

119 - UKCL

Name of the legal entity	UNIVERZITETNI KLINICNI CENTER LJUBLJANA

Expertise, available infrastructure(s)
The University Medical Centre Ljubljana is the largest hospital in Slovenia with around 10,000 employees and treats more than 100,000 patients a year. It is also a teaching hospital associated with the Medical Faculty

Ljubljana. Clinical Institute for Genomic Medicine is the only referent tertiary centre in the field of genomic medicine in the Slovene health system and has more than 55 years of experience in the diagnosis and treatment of rare diseases. We were in 2013 among the first European institutions which introduced NGS technology into the national healthcare system. Our vision is to lead the forefront in translating innovative genomic technologies into healthcare systems, thereby enhancing the diagnostic and management capabilities for rare diseases.
Main tasks in the project: Contributor: Task6.2; Task6.3;

120 - WDO

Name of the legal entity	STICHTING UNITED PARENT PROJECTS MUSCULAR DYSTROPHY
Expertise, available infrastructure(s) WDO (World Duchenne Organization) is a non-profit global organization, member of EURORDIS, RDI, EPF, and an eligible member of the European Medicines Agency, empowering direct links to regulators and rare diseases research. The organization's goals are to promote research, drug development, and advocacy, with 50+ member patient organizations across Europe and the Globe. WDO will support the project with its extensive knowledge of RD patient-centred research and patient training capacities.	
Main tasks in the project: Leader: Task4.1 Contributor: Task1.2; Task2.3; Task3.1; Task3.3; Task4.2; Task4.3; SubTask4.3.1; SubTask4.3.2; Task5.1; Task5.3; Task10.3; Task12.1; Task14.1; Task14.3; Task20.1; Subtask20.1.1; Task20.3; Subtask20.3.6; SubTask20.4.1; SubTask20.4.2; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6;	

121 - UU

Name of the legal entity	UPPSALA UNIVERSITET
Expertise, available infrastructure(s) UU is hosting the National Bioinformatics Infrastructure Sweden (NBIS) with ~120 staff, of which over 60 are bioinformatics support experts that provide advanced bioinformatics expertise in various research projects. NBIS also has ~15 systems developers to provide tools and tailored bioinformatics analytical pipelines.	
Main tasks in the project: Leader: Task15.3; Task19.4 Contributor: WP7.0; Task7.1; Task7.2; Task7.3; Task19.3;	

122 – c4c-s

Name of the legal entity	CONECT4CHILDREN STICHTING
Expertise, available infrastructure(s) conect4children (c4c) is a large, effective, pan-European research infrastructure (21 countries, 250 sites, 400 experts) that supports the design and conduct of studies that develop and improve medicines used by babies, children, and young people. c4c has grown out of a successful IHI public private partnership that has co-developed with industry and academia a number of services that facilitate the development of medicines for rare diseases in the paediatric population: site and study setup (including trial feasibility); expert advice including the perspectives of methodologists, clinicians, and people with lived experience of rare diseases; education and training about paediatric aspects of rare diseases; paediatric specificities of data standards in clinical trials. Each of these services uniquely meets a specific need for ERDERA. All staff and infrastructure are in place to carry out the ERDERA's activities.	
Main tasks in the project: Leader: SubTask20.4.3; SubTask20.4.5; Contributor: Task20.1; Subtask20.1.2; Task20.4; SubTask20.4.1; SubTask20.4.2; SubTask20.4.4; SubTask20.4.6; Task25.3;	

123 - Cadi Ayyad University

Name of the legal entity	UNIVERSITE CADI AYYAD
Expertise, available infrastructure(s)	

Cadi Ayyad University has the first Moroccan reference laboratory for conforming diagnoses in patients with rare diseases, we have conducted several studies in the most common rare diseases in Morocco, thanks to our works, several patients are currently under treatment, and clinicians are more awake to symptoms evoking rare diseases. Thanks to our expertise our laboratory and hospital receives all Moroccan patients with rare diseases and we are thus the leader of the Moroccan consortium for rare diseases. We have national registers, national biobanks relating to patients with rare diseases, which allows us to carry out different research studies
Main tasks in the project: Leader: Task24.2 Contributor: Task25.1;

124 - CNRS

Name of the legal entity	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS
Expertise, available infrastructure(s) IVETh industrial integrator (CNRS/Université Paris Cité/INSERM) is the first French technological hub dedicated to extracellular vesicles (EV) and nano vectors bioproduction, engineering and characterization for diagnosis and personalized nanomedicine. IVETh created different breakthrough technologies (10 patents, two spin off EVERZOM, Evora Biosciences) for EV scalable production (by turbulence physical stimulation in GMP bioreactors), loading with exogenous agents and local delivery. IVETh technologies include : Cell engineering (CRISPR/Cas9), Microfluidic, High yield EV production, Isolation and Loading methods (fusion with LNP), Analytical microfluidic fractionation (AF4 / MALS, DLS, RI, Fluo, UV-Vis), Quantification, sizing, phenotyping (NTA, Exoview, NanoFCM), Raman spectroscopy, super-resolution nanoscopy, AFM, HCS microscopy and organoids t. Characterization of EV quality are being correlated to their biological activity (QSAR approach and AI approach for quality control).	
Main tasks in the project: Contributor: WP21.0; Task21.3;	

125 - CIBER

Name of the legal entity	CONSORCIO CENTRO DE INVESTIGACION BIOMEDICA EN RED M.P.
Expertise, available infrastructure(s) CIBER is composed by 13 thematic areas. One of the is focused on Rare Diseases (CIBERER) is a network structure (over 700 investigators organized in 76 research and clinical groups) for translational research into rare diseases. CIBERER has the Undiagnosed Research Program, called ENoD and also coordinates the Undiagnosed Diseases Network called IMPaCT-GENóMICA. CIBER has also the capacity to develop novel viral and non-viral mediated gene editing and gene therapies of rare diseases affecting hematopoietic, epidermal, inflammatory, and metabolic diseases using in vitro and in vivo approaches and to develop lipid nanoparticles allowing the encapsulation and controlled release of mRNA. So, CIBER will participate in the Clinical Research Network activities, focusing on diagnostic-related topics, as well as National Mirror Groups in collaboration with ISCIII and also in the innovative therapies development.	
Main tasks in the project: Contributor: Task7.1; Task7.2; WP21.0; Task21.3; Task21.4;	

126 - UEFISCDI

Name of the legal entity	UNITATEA EXECUTIVA PENTRU FINANTAREA INVATAMANTULUI SUPERIOR A CERCETARII DEZVOLTARII SI INOVARII
Expertise, available infrastructure(s) UEFISCDI is participating as a funding agency in 8 different HE partnerships. As for H2020, UEFISCDI has been partner in 42 ERA-NET Cofund networks, having significant expertise on how to manage external calls and their related actions.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

127 – UNIROMA1

Name of the legal entity	UNIVERSITA DEGLI STUDI DI ROMA LA SAPIENZA
Expertise, available infrastructure(s)	

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

The Team has solid expertise in 1) structural bioinformatics and 2) teaching, training and curriculum design. 1) Research activities focus mainly on the functional interpretation of protein variants in several contexts including rare diseases, antibiotic resistance, SARS-CoV-2, and human pathologies in general. Currently the team is working on the prediction of RD mutations that can be treated with pharmacochaperons. This expertise fits in the overall ERDERA, where the Team can contribute to the study and analysis of the effects of protein variants identified by other ERDERA teams and provide structural basis and rationale for the design of new therapies. 2) Team leaders have strong competences in teaching practices and learning processes. We support academic institutions in the design of curricula, developed and annually deliver a post-graduation advanced course in bioinformatics, and are expert adviser on teachers' training for our and other universities. We lead the ELIXIR Europe Train the Trainer programme. The Team has access to computational facilities within the context of ELIXIR-IT and Sapienza Università. Moreover, the Team is equipped with workstation and servers running molecular graphics and modelling software.
Main tasks in the project: Contributor: Task6.2; Task6.3; Task20.4; SubTask20.4.1; SubTask20.4.2; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6;

128 – UANTWERPEN

Name of the legal entity	UNIVERSITEIT ANTWERPEN
Expertise, available infrastructure(s) Jonathan Baets is a neurologist and neuromuscular disease specialist; he coordinates an academic referral centre for neuromuscular diseases and is academic and clinical chair of neurology at his institution. My focus is primarily on molecular and clinical genetic studies of rare neuromuscular diseases further establishing the genetic markup of these diseases, enlarging the genotype-phenotype spectrum, pinpointing key elements in the pathophysiology of the disease and paving the way towards biomarker and therapeutic studies. We work in close collaboration with the diagnostic division of the genetics department of the Antwerp University Hospital and this allows research repurposing of large amounts of diagnostic WES datasets. In addition we extend our expertise in novel long-read whole-genome sequencing technologies in international collaboration with the University of Miami (Stephan Züchner).	
Main tasks in the project: Contributor: Task6.2; Task6.3	

129 - BNSF

Name of the legal entity	BULGARIAN NATIONAL SCIENCE FUND
Expertise, available infrastructure(s) BNSF is a research funding agency. BNSF has extensive experience with joint-funded calls and management of research projects.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

130 - Aalborg University Hospital

Name of the legal entity	Aalborg University Hospital
Expertise, available infrastructure(s) As a University hospital we receive samples for exome and genome sequencing from the entire Northern Region of Denmark. We have all necessary equipment for genetic and functional studies. We will be able to contribute as research performers, contribute to testing and validation of tests including new approaches or ideas. We have profound experience with training and education of medical/clinical geneticists, clinical laboratory geneticists/molecular biologists, and other subgroups of laboratory personnel. In research projects we are using multiomics approaches including genomics, epigenomics, transcriptomics and metabolomics.	
Main tasks in the project: Contributor: Task6.2; Task6.3;	

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

131 - RDB

Name of the legal entity	RARE DISEASES BULGARIA
Expertise, available infrastructure(s) Rare Diseases Bulgaria is the first alliance of patient organizations in the country, and its founders are organizations with many years of experience in advocacy and support for people living with rare diseases in Bulgaria. The team consists of people - patient advocates - experts in health policies, social support and inclusion, communications and financial operations. Our role will be to ensure that the "voice of the patient" and especially an underrepresented country such as Bulgaria is represented in the ERDERA in the best possible way in the interests of all partners and stakeholders. As a network of experienced organizations we have a wide range of partners in and outside the country, we are as well representing the country on the Council of the National Alliances in EURORDIS. We will work together with researchers, health and social care providers, politicians, media and families living with rare diseases to contribute to every possible aspect, including facilitating our experience and disseminating knowledge and information about the project.	
Main tasks in the project: Contributor: WP24.0; Task24.2;	

132 – BBMRI-ERIC

Name of the legal entity	BIOBANKS AND BIOMOLECULAR RESOURCES RESEARCH INFRASTRUCTURE CONSORTIUM (BBMRI-ERIC)
Expertise, available infrastructure(s) BBMRI-ERIC is a European research infrastructure for biobanks and biomolecular resources. BBMRI-ERIC has significantly contributed to EJP RD development of Virtual Platform (VP), contributing to the architecture development and subsequently focusing on integrating rare disease biobanking resources into the findability and accessibility services of the VP. This namely entails Directory (resource-level discovery) and Locator (record-level discovery). Negotiator service is now being integrated in the VP to allow access to the discovered resources and negotiate between requesters and resource providers. BBMRI-ERIC is developer and operator of these services and hence has the full capability and expertise to operate, maintain, support, and further develop these services as a part of ERDERA. BBMRI-ERIC has also supported integration of the LifeScience AAI into the VP and migration of services by other service providers in EJP RD outside of BBMRI. LifeScience AAI is a joint effort of LifeScience research infrastructures, under leadership of ELIXIR, BBMRI-ERIC and INSTUCT-ERIC.	
Main tasks in the project: Contributor: Task13.2;	

133 - Aarhus University Hospital

Name of the legal entity	AARHUS UNIVERSITETSHOSPITAL
Expertise, available infrastructure(s) Aarhus University Hospital has great expertise in clinical evaluation of patients with rare genetic conditions, the genetic analysis (WGS) in Pernille Axél Gregersen lab (core facility) and genetic variant interpretation. Pernille Axél Gregersen lab has competences within all steps of the genetic diagnostics of this patient group.	
Main tasks in the project: Contributor: Task6.2; Task6.3;	

134 – IABS

Name of the legal entity	ASSOCIATION INTERNATIONALE DE STANDARDISATION BIOLOGIQUE POUR L'EUROPE(IABS-EU)
Expertise, available infrastructure(s) The International Alliance for Biological Standardization (IABS) is an independent, non-profit scientific alliance, founded in 1955 with members in over 50 countries. IABS's mission: • To host conferences and workshops, facilitate communication, and develop consensus on key contemporary issues related to biologicals among those who discover, develop, produce and regulate biological products for human and animal health	

- To foster evidence-based Science as the standard for improving and ensuring the quality and the safety of biological products
- To share scientific advancements and innovative regulatory solutions through our journal “Biologicals”.

The cell and gene therapy committee members include current and former regulators and representatives from USP, EDQM, NIBSC, NIHS.

Main tasks in the project:
Leader: Task 18.1;

135 - HRCI

Name of the legal entity	Health Research Charities Ireland Company Limited by Guarantee

Expertise, available infrastructure(s)
HRCI will be a contributor on Task 1.2.2: PPIE. HRCI brings a strong track record and expertise in including patients as partners in research and a particular knowledge of rare disease research, through many years of involvement.
We will support many of the activities of Task 1.2.2. Our role will be to contribute expertise and practical guidance on PPIE practices. We will share our guidelines and templates, as well as our knowledge of other existing resources. We will help to shape a PPIE framework for the ERDERA, support the development of surveys and also provide a link to the Irish rare disease patient community.
We have the capacity and infrastructure to actively contribute to the ERDERA. Ireland is a leader internationally in PPIE and we are a leader in Ireland. We are an established national umbrella organisation for over 40 charities, with very strong governance, and a staff team with expertise in PPIE, patient organisations, rare disease research, communications and patient advocacy.

Main tasks in the project:
Contributor: Task1.2;

136 - LMU

Name of the legal entity	LUDWIG-MAXIMILIANS-UNIVERSITAET MUENCHEN

Expertise, available infrastructure(s)
Prof. Klopstock is the Leader of Task 9.4 Development of a blueprint and inventory of regulatory-grade natural history cohort data, as well as a Contributor in Task 9.1 Use of primary healthcare data (EHRs) for RD outcome research and Task 10.1 Platform for regulatory-grade patient-centred COA development and validation. As Coordinator of mitoNET and TIRCON and Principal Investigator of the global registry for mitochondrial disorders, he has strong expertise in setting up and analysing large registries and natural history studies. In Task 9.4, together with other contributors, we will address an important next step for academic registries and natural history studies, i.e. to establish the procedures to achieve EMA qualification for regulatory-grade natural history that may serve as an external comparator arm in non-randomized clinical trials as well as for post-authorisation safety surveillance (PASS) and efficacy (PAES) studies.

Main tasks in the project:
Leader: Task9.4
Contributor: Task9.1; Task10.1; Task14.1;
KUM :
Contributor: Task9.1; Task10.1; Task14.1;

137 - MSW

Name of the legal entity	MyScienceWork SAS

Expertise, available infrastructure(s)
MyScienceWork (MSW) is a technology company that provides a suite of data solutions for universities, research institutions, scientific publishers and private-sector R&D companies. In 2018, MSW released an open source solution for research data management named Polaris OS (available on GitHub) that has been developed with modern, open-source technologies (Elasticsearch, Node.js, Vue.js, etc.) to guarantee the project’s sustainability and openness.

For the project, MSW will implement Polaris OS as a grant management platform for calls for projects and monitoring of funded projects. The platform will be customised (forms, workflows, interfaces, analytics...) to stick to the specifics of the project.
Main tasks in the project: Contributor: Task1.3;

138 - FNR

Name of the legal entity	FONDS NATIONAL DE LA RECHERCHE
Expertise, available infrastructure(s) and role in the project The FNR has participated as a funding agency in a wide variety of international research funding collaborations, including ERA-NET programmes from H2020 and before. We have extensive experience with joint-funded calls and management of research projects.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

139 - NKFIH

Name of the legal entity	NEMZETI KUTATASI FEJLESZTESI ES INNOVACIOS HIVATAL
Expertise, available infrastructure(s) and role in the project The National Research, Development and Innovation Office (NKFIH) of Hungary is a governmental funding organization that supports R&D&I projects at universities, research institutions and SMEs within Hungary. As a research funder, the NKFIH participation in ERDERA will be aimed at participating in joint transnational (co-funded) calls for research.	
Main tasks in the project: Contributor: WP3.0; Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

140 - PEI

Name of the legal entity	BUNDESINSTITUT FUR IMPFSTOFFE UND BIOMEDIZINISCHE ARZNEIMITTEL
Expertise, available infrastructure(s) and role in the project PEI is an internationally recognized medicines agency, responsible for the regulation of biomedicinal products including gene therapy and for conducting research in related areas. Prof. Ivics is heading the Research Center at the Division of Haematology, Gene and Cell Therapy, and is a leading expert in transposon-mediated non-viral gene delivery and gene therapy. He published >160 articles and has 12 patents, several of them licensed to biotech companies. Prof. Buchholz, who is heading the Molecular Biotechnology and Gene Therapy Section at PEI, is a renowned expert on any aspects of gene transfer vectors. In particular, he invented receptor-targeted lentiviral vectors. He has published more than 100 research articles and filed several patents on this technology, which has been taken up by biotech industry. Currently, he is extending this approach to AAVs and RNA-LNPs.	
Main tasks in the project: Contributor: WP21.0; Task21.1; Task21.2; Task21.3;	

141 - PLUS

Name of the legal entity	PARIS-LODRON-UNIVERSITAT SALZBURG
Expertise, available infrastructure(s) Nicole Meisner-Kober has extensive expertise in preclinical discovery and development of RNA based drugs as well as drug delivery using extracellular vesicles, LNPs and hybrid nanovesicles. Her team at the PLUS has access to critical infrastructure for cellular and in vivo studies to advance novel types of mRNA nanoparticles, including quantitative studies of trafficking and in vivo biodistribution down to the single vesicle - single cell level. Her team will contribute to the following aims: • Mechanistic understanding of current LNPs/EVs/nanoparticles in terms of extracellular interactions and intracellular processing to enable rational design of novel mRNA/nanoparticles formulations, including sustained release • Development of tools based on AI to implement formulation design efficiency	

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• Transferable protocols for in vitro and in vivo evaluation of efficacy, pharmacokinetics, immunogenicity and safety • Demonstration of scalability of optimized mRNA formulations made with LNPs/EVs/nanoparticles • Compare and characterize PK and biodistribution from various routes of administration (i.v, i.m, i.p). Definition of regulatory quality control parameters of mRNA formulations in compliance with regulatory expectations and regulatory advice (de-risking approach to maximize the production of relevant mRNA s for clinical use)
Main tasks in the project: Contributor: WP21.0; Task21.3;

142 - SORBONNE UNIVERSITE

Name of the legal entity	SORBONNE UNIVERSITE
Expertise, available infrastructure(s) Thanks to its 135 research units, Sorbonne University brings together a scientific community of 6,400 teacher-researchers and researchers. This collective is involved in various scientific disciplines, relying on a strong intellectual tradition allowing them to address the most fundamental questions. Mobilizing disciplines ranging from the humanities to medicine through technological sciences (computer science, robotics, etc.), formal (mathematics) or natural sciences (physics, chemistry, biology, geology, etc.), Sorbonne University is a privileged crucible for tackling transversal and interdisciplinary manner the questions raised by our environment and society.	
Main tasks in the project: Leader: Task25.1 Contributor: Task20.4; SubTask20.4.1; SubTask20.4.2; SubTask20.4.3; SubTask20.4.4; SubTask20.4.5; SubTask20.4.6;	

143 - UNISI

Name of the legal entity	UNIVERSITA DEGLI STUDI DI SIENA
Expertise, available infrastructure(s) The University of Siena, in Tuscany, is one of the oldest public universities founded in Italy and one of the oldest in the world. First called Studium Senese, it was established in 1240 with the faculties of medicine and law. With nearly 20,000 students1, it brings together almost half of the city's total population, which represents 54,000 people. Today, the University of Siena is mainly known for its faculties of literature and philology, law and medicine.	
Main tasks in the project: Contributor: Task6.2; Task6.3;	

144 - VINNOVA

Name of the legal entity	VERKET FOR INNOVATIONSSYSTEM
Expertise, available infrastructure(s) Vinnova – is Sweden’s innovation agency. Vinnova will participate in cofunding activities as well as to create synergies with other partnerships and instruments to accelerate further development and innovation. Vinnovas mission is to promote sustainable growth by improving the conditions for innovations, as well as funding needs-driven research. Vinnova also supports the private sector focusing on SMEs as well as demonstrations/pilots and mission driven approaches. Every year Vinnova invests about SEK 3 billion in various initiatives. Since co-financing from actors must total at least the same amount, the funds for addressing societal challenges are doubled. In addition, Vinnova is the Swedish Government's expert authority in innovation policy.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

145 – CRG-CERCA

Name of the legal entity	FUNDACIO CENTRE DE REGULACIO GENOMICA
Expertise, available infrastructure(s) CRG will provision research and technology infrastructure and perform research. CRG was part of EJP RD, consortium built to create a comprehensive, sustainable ecosystem allowing a virtuous circle between research, care, and medical innovation. In the project "Gene Environment interactions in Mental health trajectories of Youth (Youth-GEMs)" (Funded by Horizon Europe programme.) aiming to characterize how the interplay between genetic, cognitive, social, and environmental factors is impacting mental health, CRG, as WP lead, is handling data management, discovery, and access aspects of the project. CRG is also part of ELIXIR-CONVERGE (H2020), EASI-Genomics (H2020) and EOSC4Cancer (HEurope) The European Genome-phenome Archive (EGA) is a global network for permanent archiving and sharing of personally identifiable genetic, phenotypic, and clinical data generated for the purposes of biomedical research projects. EGA enables proper Data Management of sensitive data.	
Main tasks in the project: Contributor: WP6.0; Task14.2;	

146 – GMS-Skane Region

Name of the legal entity	Section of Clinical Genetics, Dept of Clinical Genetics, Pathology and Molecular Diagnostics, Region Skåne, Sweden
Expertise, available infrastructure(s) Clinical Genetics Lund is a provider of relatively large volumes of clinical WGS data, and that we are mainstreaming the procedure to allow for research consent for the majority of patients. We are eager to participate in data sharing to increase clinical yield, but we see some regulatory hurdles in Sweden. With our commitment to the national project GMS and specifically NGP, we see a possibility to participate both in building and testing a format for European collaboration through federated data access, but also to provide clinical data for the entire project.	
Main tasks in the project: Contributor: Task6.2; Task6.3; Task7.3;	

147 - VIB

Name of the legal entity	VLAAMS INSTITUUT BIOTECHNOLOGIE FLANDERS INSTITUTE FOR BIOTECHNOLOGY
Expertise, available infrastructure(s) Sarah Weckhuysen is a neurologist at the University Hospital of Antwerp, an Associate Professor at the University of Antwerp in Belgium, and leader of the Weckhuysen team at the VIB-Center for Molecular Neurology in Antwerp. The primary focus of her research group is the identification of novel genes and genetic mechanisms implicated in monogenic epilepsy. Her team has contributed to the discovery of > 20 novel disease genes, placing our group at the international forefront of epilepsy genetics research. They work closely together with the diagnostic Center for Medical Genetics of the University Hospital, where diagnostic exome sequencing is performed. Their group has access to the diagnostic exomes allowing re-analysis in a research setting. Their research centre is a leader in data generation and analyses on the Oxford Nanopore sequencing platform (ONT), has developed several open access software packages and established the Long Read Sequencing Expert Unit (2023)	
Main tasks in the project: Contributor: Task6.2; Task6.3;	

148 – IPG

Name of the legal entity	INSTITUT DE PATHOLOGIE ET DE GENETIQUE
Expertise, available infrastructure(s) IPG is a non-profit foundation for diagnosis, education & research. IPG has unique experience & expertise in pathology, clinical genetics, molecular & cell biology medical diagnosis. The Centre of Human Genetics provides full services in the diagnosis, treatment & management of hereditary disorders & birth defects affecting foetuses, newborns, children, adolescents & adults. A wide variety of clinical services is proposed including a	

general genetics clinic, metabolic clinic, renal genetic clinics, autism/medical genetics clinic & intellectual disability evaluations. IPG is well-equipped with core facilities including a biobank cell & molecular imaging, a molecular genetics laboratory (equipped w.1 MiniSeq,1MiSeq,3 NextSeq500,1 NovaSeq6000…) & a bioinformatic unit with experience in analysing high throughput sequencing data.
Main tasks in the project: Contributor: Task6.2; Task6.3;

149-UO

Name of the legal entity	UNIVERSITY OF OTAGO
Expertise, available infrastructure(s) Associate Professor Louise Bicknell is a molecular geneticist and has a significant track record in identifying and characterising genetic causes of rare disorders, particularly focused on Meier-Gorlin syndrome and neurodevelopmental disorders. Her research uses genomics and molecular biology tools to generate evidence in support of variant pathogenicity for both novel and established genes. She is Co-Director of Genetics Otago, a virtual research centre supporting > 400 genetics researchers from University of Otago, and is a member of the Human Genetics Society of Australia-New Zealand Branch Executive Committee. She will lead the New Zealand National Mirror Group, and represent New Zealand in this consortium.	
Main tasks in the project: Contributor: Task6.2; Task6.3; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;	

150 – HSJD

Name of the legal entity	HOSPITAL SANT JOAN DE DEU
Expertise, available infrastructure(s) Hospital Sant Joan de Déu in Barcelona is a leading healthcare facility known for its specialization in paediatrics, obstetrics, and gynaecology. It is affiliated with the University of Barcelona and stands as one of Europe's premier medical institutions dedicated to children's health. The hospital is renowned for its comprehensive range of medical services, innovative research programs, and commitment to compassionate care. Additionally, it serves as a vital centre for maternal and child health, offering advanced treatments and support for families. Since 01/09/2023, this organization is coordinating the European Reference Network EpiCare (https://epi-care.eu/) for rare and complex epilepsies. It is co-leading the task 25.4 dedicated to ensuring alignment of ERDERA with the Research strategies of the European Reference Networks.	
Main tasks in the project: Leader: Task 25.4 Contributor: Task25.1;	

Associated Partner 151 - AZ

Name of the legal entity	ASTRAZENECA AB
Expertise, available infrastructure(s) Cas9 off-target analysis in vivo AZ work on CRISPR/Cas9 gene editing technology aimed to investigate the potential off-target effects and the determinants of indels (insertions and deletions). Published studies found that off-target effects were rare but could occur, and suggested that using more precise guide RNAs and optimizing delivery methods could reduce their frequency. Cas9 indels profiling A published study analysed a large dataset of CRISPR/Cas9 editing events and found that the frequency and size of indels were influenced by the target sequence, guide RNA, and cell type being edited. The study concluded that predicting and controlling the frequency and size of indels could improve the accuracy and safety of CRISPR/Cas9 gene editing. Development of Prime Editing Nucleases	

A published study introduces two strategies for precise genomic insertions using SpCas9 nuclease-based prime editor. First method combines PEn with pegRNAs for homology-dependent DSB repair, and inhibits unintended edits by DNA-PK inhibition. Second method utilizes springRNAs for NHEJ-mediated integrations. PEn editing is effective for small genomic insertions/deletions and SNV repair and expands spectrum of DNA repair mechanisms for prime editing. Genome Engineering Fully equipped tissue culture and molecular biology labs. The labs are fully equipped with gel electrophoresis systems, microcentrifuges, PCR machines, and other routinely used molecular biology and tissue culture equipment. NGS & Transcriptomics The NGS and Transcriptomics group is fully equipped for support of Next Generation Sequencing with access to MiSeq, NextSeq, Fluidigm, OXford Nanopore, QPCR, ddPCR and automation assistance to support molecular biology work. Bioanalysis The Bioanalytical team is fully equipped to support the discovery of biological entities and their development into novel therapeutics using bespoke qualitative and quantitative assays.
Main tasks in the project: Leader: Task18.2 Contributor: Task 18.1; WP21.0; Task21.2; Task21.3; Task21.4; Task21.5;

Associated Partner 152 – CHEO-RI

Name of the legal entity	CHILDREN'S HOSPITAL OF EASTERN ONTARIO RESEARCH INSTITUTE INC
Expertise, available infrastructure(s) The Boycott Lab aims to understand the molecular pathogenesis of the most-difficult-to-solve rare diseases. She leads the Care4Rare Canada Consortium, worked with the Ontario Ministry of Health to integrate genomics as a publicly funded test for rare disease diagnosis, and is co-PI of the Rare Diseases: Models & Mechanisms Network. The Lochmüller Lab studies neuromuscular disorders (esp. congenital myasthenic syndrome, myotonic dystrophy) from basic (pathways, biomarkers, drug screening) to clinical (natural history, clinical trials). He leads NMD4C (neuromuscular disease network for Canada) and coordinated international networks (IRDiRC Interdisciplinary Scientific Committee), consortia (RD-Connect) and biobanks (EuroBioBank). lHL will advance his treatabolome work and contribute genomic data for reanalysis and discovery (16.3,6.3,8.2); KB will contribute to matchmaking (15.3); and both will network with ERDERA (25.3) and share expertise in data sharing and reanalysis (6.2,6.3,7.1,7.3).	**Expertise, available infrastructure(s)** The Boycott Lab aims to understand the molecular pathogenesis of the most-difficult-to-solve rare diseases. She leads the Care4Rare Canada Consortium, worked with the Ontario Ministry of Health to integrate genomics as a publicly funded test for rare disease diagnosis, and is co-PI of the Rare Diseases: Models & Mechanisms Network. The Lochmüller Lab studies neuromuscular disorders (esp. congenital myasthenic syndrome, myotonic dystrophy) from basic (pathways, biomarkers, drug screening) to clinical (natural history, clinical trials). He leads NMD4C (neuromuscular disease network for Canada) and coordinated international networks (IRDiRC Interdisciplinary Scientific Committee), consortia (RD-Connect) and biobanks (EuroBioBank). HL will advance his treatabolome work and contribute genomic data for reanalysis and discovery (16.3,6.3,8.2); KB will contribute to matchmaking (15.3); and both will network with ERDERA (25.3) and share expertise in data sharing and reanalysis (6.2,6.3,7.1,7.3).
Main tasks in the project: Contributor: Task6.2; Task6.3; WP7.0; Task7.1; Task7.3; Task7.4; Task8.2; Task25.3;	

Associated Partner 153 - CIHR

Name of the legal entity	CANADIAN INSTITUTES OF HEALTH RESEARCH
Expertise, available infrastructure(s)	

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As the main federally funded health-research funding agency in Canada, and given our track record of collaboration with European partners in various work programs, CIHR possess all the expertise required to ensure a successful Canadian participation to the ERDERA. Our main role will be to contribute to all the aspects of the JTCs. In addition, we will ensure alignment of the Clinical Research Network with the Paediatric Rare DIsease Clinical and Treatment Network that is currently being established in Canada through CIHR's funding. Additionally, CIHR will be contributing to the alignment of the ERDERA activities with other like-minded International activities. As part of Government of Canada structure, CIHR have the required financial and human resources to fully contribute to the ERDERA activities as a partner not receiving funding from the EC.
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5; Task25.1;

Associated Partner 154 - DFG

Name of the legal entity	DEUTSCHE FORSCHUNGSGEMEINSCHAFT EV
Expertise, available infrastructure(s) DFG is a research funding agency. DFG has participated as a funding agency in previous international research funding collaborations, including EJP RD. DFG has extensive experience with joint-funded calls and management of research projects.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

Associated Partner 155 – FDB

Name of the legal entity	FUJIFILM DIOSYNTH BIOTECHNOLOGIES UK LIMITED
Expertise, available infrastructure(s) Fujifilm Diosynth is a contract development and manufacturing organisation (CDMO) operating from multiple sites across the World. We support numerous groups developing biologics and ATMPs across all clinical and commercial scales. We will bring this real world experience in supporting the translation of ideas into viable, manufacturable products to the project providing feedback on impact and likely adoption of proposed approaches. We may test or demonstrate emerging technologies in an industry setting and may wish to license emerging technologies which we believe will improve the translation, manufacture or understanding of ATMPs.	
Main tasks in the project: Contributor: Task 18.1; WP21.0; Task21.1; Task21.2; Task21.3; Task21.4;	

Associated Partner 156 - FRQS

Name of the legal entity	FONDS DE RECHERCHE DU QUEBEC - SANTE
Expertise, available infrastructure(s) The FRQS is the main provincial funding agency in human health research in Québec and reports to the Minister of Economy, Innovation and Energy. Its mission is to support health research to foster the wellness of Québec's population. Its mandate is to promote and financially support such research, to disseminate knowledge and train students and researchers, to forge the partnerships necessary for the development of Quebec's research and innovation system, and, lastly, to advance research internationally. FRQS allocates around $110 million annually in awards and grants in all areas of research in the field of health, including sustainable health - research carry out in universities and public health social and services sector (clinical/hospital). FRQS also aims to foster the development of collaborative research in Canada and internationally. Over the past years, FRQS participated in many ERA-Net calls as well as other joint translational calls with European countries since 2010.	
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

Associated Partner 157 - HIPRA

Name of the legal entity	HIPRA HUMAN HEALTH SL
Expertise, available infrastructure(s) Hipra has a wide experience in developing vaccines for animal health and also recently for human health. Hipra has a portfolio of vaccines for different animal species and a vaccine registered for humans Bimervax to prevent Covid-19. Hipra is able to work with different platform technologies: live and inactivated virus and bacteria,	

vectorized, recombinant proteins, VLPs. In Hipra we work from the very beginning of the research and development, the scale up, the production in our GMP manufacturing facilities, and we also work on the regulatory process for the product registration both in EU and abroad. Hipra is currently working on the mRNA technology so Hipra's role in this project could be to provide either research and development or regulatory advice in the different areas in which this is performed. Hipra also have top GMP qualified manufacturing facilities that could be available for the consortium in case it is needed to produce clinical or industrial batches.
Main tasks in the project: Contributor: Task 18.1; WP21.0; Task21.2; Task21.3; Task21.4;

Associated Partner 158 – LAB HIPRA

Name of the legal entity	LABORATORIOS HIPRA SA
Expertise, available infrastructure(s) Manufacturing facilities "HV5: DS production with 50, 200 and 500L single-use bioreactors for cell lines (CHO, HEK293, CAP, insect cells, VERO). Downstream process equipment. CB4: site with bioreactors of 100 to 2000L to grow E.coli and yeast. Downstream process equipment. VH1+VH2: blending (DP), and filling." State-of-the art facilities Manufacturing facilities equipped with the latest technologies in the biotech and processes complying with European Union GMPs regulations for the manufacturing of biological and pharmacological products. Dedicated lines and units for the production of veterinary and human vaccines.	
Main tasks in the project: Contributor: Task 18.1; WP21.0; Task21.2; Task21.3; Task21.4;	

Associated Partner 159 - MICYRN

Name of the legal entity	Maternal Infant Child and Youth Research Network
Expertise, available infrastructure(s) In response to a RFA recently launched by CIHR for a RD Clinical Trials and Treatment Network, MICYRN is leading a grant application to be submitted in October 2023. Should the proposal be funded in 2024, the proposed network will be comprised of clinical trial experts, patient and family partners, rare disease specialists including precision medicine and genomics, disease specific organizations, regulatory and health technology assessment bodies, industry partners, and institutional and operational leads from across the country. The overall coordination and facilitation of the Network will be led by MICYRN, a national organization joining 21 maternal-child health research organizations, and more than 25 affiliated practice-based research networks of investigators. MICYRN will contribute to the development of a multi-national infrastructure to support global RD paediatric trials and the sharing of knowledge. MICYRN was recently recognized at the Canadian National Mirror Group for Rare Diseases in the European Joint Programme for Rare Disorders.	
Main tasks in the project: Contributor: WP23.0; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3;	

Associated Partner 160 - MILTENYI

Name of the legal entity	MILTENYI BIOTEC BV & CO KG
Expertise, available infrastructure(s) Miltenyi Biotec is one of the world's leading providers of products and services for biomedical research and cell and gene therapy. Miltenyi has more than 4,500 employees in 28 countries worldwide and its products been used in more than 80,000 cell therapy procedures. In recent years, Miltenyi has established a broad product portfolio in this area and also was involved with numerous translational medicine projects and trials around the world. With its proprietary, fully automated, GMP-conform CliniMACS Prodigy platform, Miltenyi can perform various specialized procedures including the HSCE process (Hematopoietic Stem Cell Engineering). Similarly, Miltenyi has outstanding products for immunohistochemistry and immunofluorescence (MACSima Imaging System) and flow cytometry (MACSQuant).	
Main tasks in the project:	

Leader: Task 18.1; Task21.4 Contributor: WP21.0; Task21.1; Task21.2; Task21.3; Task21.5;

Associated Partner 161 - PFIZER

Name of the legal entity	PFIZER INC
Expertise, available infrastructure(s) At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. Pfizer strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Pfizer aims to bring experts from the following groups to the project: Rare Disease Medical, Emerging Science & Innovation Research, R&D Drug Safety, Regulatory, Digital, and Government Affairs to provide their experience in drug discovery and clinical development, cell-based assays, preclinical in vivo experimentation, next-generation sequencing, high-resolution microscopy, regulatory, medical, policy, biobanking, computational and digital sciences and analytic tool implementation and deployment. Pfizer will be the lead industry partner in the Regulatory WP (18) and Technology Accelerator (WP21) and contributing to ATMPs CRN (WP11), RD-VP (WP13), Policy (WP1).	
Main tasks in the project: Leader: **WP18.0**; **WP21.0**; Task21.2; Task21.3; Task21.5 Contributor: Task11.2; Task13.1; Task 18.1; Task21.4;	

Associated Partner 162 – RCC (Rare Care Center)

Name of the legal entity	DEPARTMENT OF HEALTH GOVERNMENT OF WESTERN AUSTRALIA
Expertise, available infrastructure(s) The Rare Care Centre (RCC) combines excellence in rare diseases diagnosis, treatment, cross-sector care coordination, digital health, computational phenotyping, trials, mental health, social services, education and workforce capacity, policy and legislation, and patient engagement and support. Combined with access to local and internationally connected research and innovation infrastructures and capacity, it is poised for significant impact on all WPs. Prof Baynam's roles have/ do include Medical Director, RCC, Chair, Diagnostics Committee, IRDiRC; Chair, Interdisciplinary Committee, IRDiRC; Co-Founder, UDNI; Founder, UDP WA, Director, Lyfe Languages; Founder, Cliniface; Co-Chair, Standards of Practice, Global Commission for Rare Diseases (RD); Member, Orphanet Australia National Advisory Board. Prof Groza is a world leader in computational phenotyping for RD and Co-chair RD, GA4GH. Prof Lassmann has led RD empowering algorithm development and multiomics in 3 continents.	
Main tasks in the project: Contributor: Task9.3; Task12.1; Task25.1; Task25.3;	

Associated Partner 163 - REI

Name of the legal entity	REITHERA SRL
Expertise, available infrastructure(s) ReiThera Srl is a CDMO company based in Rome (Italy) dedicated to technology/process development and GMP manufacturing of viral vectors for advanced therapies. The GMP facility, equipped with 50-2000L stirred-tank and fixed-bed bioreactors, also comprises a filling suite and quality control laboratories. The Process Development (PD) laboratory has extensive experience on upstream and downstream Adeno-Associated Virus (AAV) vectors production processes based on state-of-the-art technologies, aimed at increasing process yield with improved potency and purity of the vector lots. As such, ReiThera is highly suited to be part of the network of ERDERA innovative industry partners that will cooperate to the advance of cost-effective and harmonized AAV gene therapy for rare genetic diseases across Europe, through the development and standardization of a base manufacturing process in suspension cells, and the characterization of AAV vectors by more accurate, fit-for-purpose analytical methods.	
Main tasks in the project: Contributor: WP21.0; Task21.1;	

Associated Partner 164 - RJF

Name of the legal entity	LABORATORIO REIG JOFRE SA

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Expertise, available infrastructure(s) RJF is pharmaceutical company with extensive experience in product development and manufacturing of injectable products. RJF has an innovation team that leads open innovation and collaborations in the development of complex injectables and lyophilizates which has a strong experience in formulation stabilization of complex products, as well as analytical development of biological products. Also with support the quality and regulatory team for the medicinal requirements an engineering teams specialized in sterile process and biotechnological products production eRJF has a strong experience in galenic, analytical development, innovative formulations as well as in regulatory process in order to develop products from conception to clinical and commercial phases. We can contribute to the process and product characterization, quality requirements to prepare batches for clinical use and in the communication to support the project needs and maximize dissemination and access to results.
Main tasks in the project: Contributor: Task 18.1; WP21.0; Task21.2; Task21.3; Task24.3;

Associated Partner 165 – ROCHE

Name of the legal entity	F. HOFFMANN-LA ROCHE AG
Expertise, available infrastructure(s) Roche and Spark, together, are industry leaders in the development and commercialization of pharmaceutical products, including ATMPs. In 2017, Spark launched Luxturna (voretigene neparvovec-rzyl) an AAV vectored gene therapy for Leber congenital amaurosis. Roche has extensive experience of developing and commercializing products for rare diseases including: Hemlibra (emicizumab) for Haemophilia A; Evrysdi (risdiplam) for Spinal Muscular Atrophy and Enspryng (satralizumab) for Neuromyelitis Optica Spectrum Disorder (NMOSD). With end-to-end capabilities, from early discovery to global commercialization, Roche/Spark is able to tap into extensive technical resources and industry knowledge in support of this project. Roche/Sparks expertise in fundamental science, drug development and global regulatory approval positions us to provide critical support and leadership to our designated work packages.	
Main tasks in the project: Contributor: Task13.1; Task 18.1; WP21.0; Task21.1; Task21.5;	

Associated Partner 166 - SNSF

Name of the legal entity	SCHWEIZERISCHER NATIONALFONDS ZUR FORDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG
Expertise, available infrastructure(s) Based on a government mandate, the Swiss National Science Foundation (SNSF) supports scientific research in all academic disciplines – from physics to medicine to sociology. At the end of 2022, the SNSF was funding 5500 projects involving more than 20,000 researchers. This makes us the leading Swiss organisation for the promotion of scientific research. To ensure its independence, the SNSF was established in 1952 as a private foundation. Its core task is the evaluation of research proposals. By awarding public research money based on the principle of competition, the SNSF contributes to the high quality of research in Switzerland. In close collaboration with higher education institutions and other partners, the SNSF strives to create the best possible conditions for the development and global interconnectedness of Swiss research. It pays particular attention to the promotion of early-career researchers.	**Expertise, available infrastructure(s)** Based on a government mandate, the Swiss National Science Foundation (SNSF) supports scientific research in all academic disciplines – from physics to medicine to sociology. At the end of 2022, the SNSF was funding 5500 projects involving more than 20,000 researchers. This makes us the leading Swiss organisation for the promotion of scientific research. To ensure its independence, the SNSF was established in 1952 as a private foundation. Its core task is the evaluation of research proposals. By awarding public research money based on the principle of competition, the SNSF contributes to the high quality of research in Switzerland. In close collaboration with higher education institutions and other partners, the SNSF strives to create the best possible conditions for the development and global interconnectedness of Swiss research. It pays particular attention to the promotion of early-career researchers.
Main tasks in the project: Contributor: Task3.1; Task3.2; SubTask3.2.1; SubTask3.2.2; SubTask3.2.3; SubTask3.2.4; SubTask3.2.5;	

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Associated Partner 167 - UCB

Name of the legal entity	UCB BIOPHARMA

Expertise, available infrastructure(s)
Serving rare patient populations with a high amount of remaining unmet medical need is core to UCB's Patient Value Strategy. UCB has recently launched novel therapeutics in myasthenia gravis and rare forms of epilepsies (see above), with multiple additional rare disease indications in the late stage development pipeline. Overall, ~30% of UCB's end to end R&D portfolio is targeting rare diseases. UCB's recent investments in AAV-gene therapy will offer a key tool to ensure a continued flow of novel solutions & therapeutics tackling the high unmet need remaining with rare disease patients. One of the key remaining hurdles to ensure the long-term sustainability of AAV-GT as a widespread & equitable modality are elevated manufacturing costs. Interestingly, beyond improving process yields, innovation & industry-wide standardization of process analytical technologies would offer a key lever to optimize QC needs (~volume), enable consistent quality (~safety), and drive wide-spread access for patients. As such, UCB will focus its contributions specifically on the AAV tasks and associated regulatory efforts. Beyond lending its expertise, UCB has offered to conduct some analytical measurements in context of the AAV tasks, leveraging its established in house infrastructure & capabilities.

Main tasks in the project:
Contributor: Task 18.1; WP21.0;

Associated partner 168 - FRAUNHOFER UK

Name of the legal entity	FRAUNHOFER UK RESEARCH LIMITED

Expertise, available infrastructure(s)
The European Bank for induced pluripotent stem cells (EBiSC), a non-profit iPSC repository, has an established infrastructure for the ethical and legal governance, collection, qualification and distribution of iPSCs and derived cells (e.g. iPSC-neurons) from diverse sources worldwide, as well as secure data management of iPSC lines and associated datasets, including personal data. Through a multitude of long-term and ongoing collaborations, EBiSC has extensive expertise in how researchers can integrate ethical and legal governance into their research projects to enable and simplify sharing and dissemination of research tools and data. Within ERDERA, we will share this knowledge and expertise through dedicated training sessions which will highlight common issues and implementable solutions for the safeguarding and sharing of both cells and data, aiming to increase awareness and ultimately, to expand access to these critical resources.

Main tasks in the project:
Fraunhofer UK
Leader: SubTask20.3.3
Contributor: Task20.3;

Associated partner 169 – GA UK

Name of the legal entity	GENETIC ALLIANCE UK LTD

Expertise, available infrastructure(s)
PPIE: We will collaborate with other rare condition support networks in this proposal to ensure all activities have the necessary Patient and Public Involvement and Engagement contributions, ensuring compatible lived-experience, expertise and knowledge are available to inform research activities.
Training: We will provide advice and support to those in need of PPIE to ensure the teams are able to deliver best practice engagement.
Networking: We will support mirror groups to access people living with rare conditions in the UK and those that support them.

Main tasks in the project:
Contributor: Task1.2; Task5.1; Task5.3; Task20.1; Subtask20.1.1; Task20.3; SubTask20.3.4;

Associated partner 170 - UNEW

Name of the legal entity	UNIVERSITY OF NEWCASTLE UPON TYNE

Expertise, available infrastructure(s)

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The Newcastle University (UNEW) team performing this work is based in the John Walton Muscular Dystrophy Research Centre (JWMDRC). UNEW is one of the top research-intensive universities in the UK: ranked 15th (out of 157) in the UK for research power. The JWMDRC is a clinical and research centre led by Prof. Volker Straub, providing a depth of clinical expertise in Muscular Dystrophies unparalleled elsewhere in the UK. Newcastle houses the MRC Translational Research Centre for Neuromuscular Diseases and Biobank, established with UCL (London). UNEW will co-lead WP23 on '(Inter)National capacity alignment', which will ensure the alignment of European and national RD research policies. UNEW will support the establishment and maintenance of NMGs. The team has a recognised reputation in developing policy recommendations and national frameworks for rare diseases, through leading projects such as Rare 2030, RD Action, and the 'State of the Art of Rare Diseases Activities in Europe' resource. In addition, UNEW will support task 7.3 bringing expertise from genomics projects such as SOLVE-RD and MYO-SEQ.
Main tasks in the project: Leader: **WP23.0**; Task23.2; SubTask23.2.1; SubTask23.2.2; SubTask23.2.3; SubTask23.2.4; Task23.3; SubTask23.3.1; SubTask23.3.2; SubTask23.3.3 Contributor: Task6.2; Task6.3; Task7.1; Task7.3; Task23.1; SubTask23.1.1; SubTask23.1.2; SubTask23.1.3;

Associated partner 171 – CUH

Name of the legal entity	Cambridge University Hospitals NHS Foundation Trust
Expertise, available infrastructure(s) The NIHR Rare Diseases BioResource (Chief Investigator John Bradley; leads Patrick Chinnery and Willem Ouwehand) with ~23,000 patients covering 80 rare diseases supports discovery of unknown aetiological genetic variants and disease mechanisms, with the goal of improving treatment. The BioResource led the rare diseases pilot for Genomics England, demonstrating for the first time the utility of whole-genome sequencing (WGS) in a national health system (Turro et al, 2020). The Next Generation Children's project demonstrated the utility of rapid WGS in Neonatal and Paediatric Intensive Care Units (NICU and PICU), leading to implementation of rapid WGS for critically ill children within the NHS. The NIHR BioResource has established systems for patients to propose diseases for adoption and research projects that can be supported by the BioResource.	
Main tasks in the project: Contributor: WP8	

Associated partner 172 - ULEIC

Name of the legal entity	UNIVERSITY OF LEICESTER
Expertise, available infrastructure(s) Previous notable discoveries made in the host Department of Genetics & Genome Biology at ULEIC include the discovery and development of DNA fingerprinting, and the DNA-based identification of the remains of King Richard III. The ULEIC team (12 members - 7M, 5F) have experience leading international data standards such as GA4GH Beacon, GA4GH ADA-M, IRDiRC DUC/CCE (central to WP13), leading the development of the Solve-RD data platform (being extended in WP15), leading on a large Data Hub 'Workbench' platform for dementia with Gates Ventures and IMI (informing cloud and network developments in WP15), and leading on the query/discovery portal of EJP-RD (being extended in WP13). More specifically, ULEIC will contribute to Task 13.1, and will co-lead Task 15.1. ULEIC provides the RD-Nexus discovery software, now adopted by various ERNs and biobanks. This software has been integrated into Molgenis registries and into the Solve-RD data infrastructure (core to WP15), and it will continue to support the wider ecosystem that feeds the WP13 data hub. Finally, ULEIC will contribute its wider expertise on data discovery for genomics, clinical data, and patient matchmaking.	
Main tasks in the project: Leader: Task15.1 Contributor: Task13.2; Task13.3;	

Associated partner 173 - QUB-UK

Name of the legal entity	THE QUEEN'S UNIVERSITY OF BELFAST
Expertise, available infrastructure(s)	

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Dr Mone PhD MSc FRCPI MRCOG is dual qualified in foetal medicine and prenatal genomics. She is a clinical lecturer and consultant in foetal medicine. She is editor for Ultrasound in Obstetrics and Gynaecology related to genetics manuscripts primarily and also serves as an invited ISUOG faculty member. Dr Mone demonstrates international expertise in prenatal genomics by serving as a co-chair for the ISPD SIG on foetal Imaging and Phenotyping, organising and chairing relevant sessions for ISPD as well as performing abstract judging and being involved in providing educational sessions. She is elected abstract co-ordinator for the British Maternal foetal Medicine Society where she organises the annual conference and is a committee member for the foetal Genomics Group of the British Society of Genomic Medicine. Dr Mone is currently an elected member of the RCOG scientific impact committee. Dr Mone will be a PI within the proposed study.
Main tasks in the project: Leader: Task4.1 Contributor: Task7.2; Task10.3; Task13.2;

Associated partner 174 – UCL

Name of the legal entity	UNIVERSITY COLLEGE LONDON
Expertise, available infrastructure(s) UCL will contribute with OGM technology to help diagnose RD patients, having experience using past 2 years and 4 publications are under review showcasing their work. UCL also have Long-read sequencing publications.	
Main tasks in the project: Leader: Task8.3 Contributor: Task6.2; Task6.3;	

Associated partner 175 - UCAM

Name of the legal entity	Department of Clinical Neurosciences, University of Cambridge
Expertise, available infrastructure(s) The third largest department in the Cambridge School of Clinical Medicine, the Department of Clinical Neurosciences (https://www-neurosciences.medschl.cam.ac.uk/) hosts over 290 staff within 30 research groups focused on understanding the nervous system in health and disease. The aim is to harness this understanding to develop new treatments for incurable neurological and related disorders. The Department provides a rich environment for translational scientists, including groups led by both basic and clinical scientists spanning from the molecule through to neurons in networks, and the functioning brain and nervous system in health and disease. The Department promotes inter-disciplinary research at all levels, leveraging the opportunities available on Europe's largest Biomedical Campus within one of the world's leading Universities. The Department currently attracts in excess of £11 million grant funding annually, primarily from the Medical Research Council, Wellcome Trust, National Institute for Health Research, European Union and National Institutes of Health. The project will be done in collaboration with the MRC Mitochondrial Biology Unit (MBU), which is part of the Department of Clinical Neurosciences. MBU is a world-recognised centre for the study of mitochondrial medicine and biology. The third largest department in the Cambridge School of Clinical Medicine, the Department of Clinical Neurosciences (https://www-neurosciences.medschl.cam.ac.uk/) hosts over 290 staff within 30 research groups focused on understanding the nervous system in health and disease. The aim is to harness this understanding to develop new treatments for incurable neurological and related disorders. The Department provides a rich environment for translational scientists, including groups led by both basic and clinical scientists spanning from the molecule through to neurons in networks, and the functioning brain and nervous system in health and disease. The Department promotes inter-disciplinary research at all levels, leveraging the opportunities available on Europe's largest Biomedical Campus within one of the world's leading Universities. The Department currently attracts in excess of £11 million grant funding annually, primarily from the Medical Research Council, Wellcome Trust, National Institute for Health Research, European Union and National Institutes of Health. The project will be done in collaboration with the MRC Mitochondrial Biology Unit (MBU), which is part of the Department of Clinical Neurosciences. MBU is a world-recognised centre for the study of mitochondrial medicine and biology.	
Main tasks in the project: Contributor: Task6.2; Task6.3; Task8.4;	

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Work that is going to be performed by associated partners (Article 9.1 of the MGA)	
151 – AZ	*See description of their planned activities above*
152 – CHEO-RI	
153 – CIHR	
154 – DFG	
155 – FDB	
156 – FRQS	
157 – HIPRA	
158 – LAB HIPRA	
159 – MICYRN	
160 – Miltenyi	
161 – Pfizer	
162 – RCC	
163 – REI	
164 – RJF	
165 – ROCHE	
166 – SNSF	
167 – UCB	
168 – Fraunhofer UK	
169 – GA UK	
170 – UNEW	
171 – CUH	
172 – ULEIC	
173 – QUB-UK	
174 – UCL	
175 – UCAM	

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Budget considerations:
The estimation of the overall budget of ERDERA, including 3 years and 7 years instalments is presented below. The total budget corresponds to the overall cost of the activities, while the EC request corresponds to the expected reimbursement. It is important to underline that the difference between total and EC request corresponds to the minimum *in-kind* contribution to be provided by the partners. It is expected that this *in-kind* contribution will be higher than indicated since the sum of indicative *in-kind* commitments summarized in the Letters of Intents of 91 organisations from 29 countries amounted at 156.7 Million €.
In that way, the ERDERA consortium ensures that overall, *in cash* and *in-kind* commitments to the programme will be sufficient to cover the total costs of the activities, but also to obtain the expected reimbursement of the EC planned for 3 + 7 years (around 150 Million €).

In addition, ERDERA comprises 18 Associated Partners (industry and public funding bodies) that jointly committed 13.76 Million €. These budgets are indicated in the table below. All Associated Partners are fully committed to ERDERA, which is reflected by their direct participation in different WPs and tasks and will be formalised additionally within the Consortium Agreement.

	7 years project		1st instalment (Year 1 - 3)	
	Total Cost	EC Requested	Total Cost	EC requested
Coordination & Strategy	18 609 020 €	16 650 618 €	8 493 937 €	7 582 293 €
RD Funding	244 886 552 €	61 329 697 €	98 343 411 €	10 790 656 €
Clinical Research Network	50 734 575 €	35 514 203 €	26 398 175 €	18 478 723 €
Data Services Hub	20 125 025 €	14 087 517 €	7 877 669 €	5 514 368 €
Expertise Services Hub	5 335 450 €	3 734 815 €	2 168 450 €	1 517 915 €
Education & Training Hub	8 643 325 €	6 050 328 €	3 524 332 €	2 467 033 €
Acceleration Hub	23 408 401 €	10 500 500 €	12 405 501 €	5 467 765 €
Inter(national) Capacity Alignme	13 886 916 €	12 101 121 €	5 897 421 €	5 110 520 €
Total	**385 629 264 €**	**159 968 798 €**	**165 108 895 €**	**56 929 273 €**

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2.1. Resources to be committed.

2.1.1. Summary effort table

Table 2.3.d: Summary of staff effort <u>for Year 1</u> (Leaders in bold)

The number of PMs per partner reflects the total effort of the partner. However, the number of PMs corresponding to INSERM includes also the PMs put aside as "central budget" and that will be allocated during the programme run according to task definition and assignment to specific partners.
The low number of PMs for some beneficiaries is related to the fact that some budgets will be allocated at later stage and thus (potentially) distributed to those partners. Nevertheless, their participation was considered as essential from the start of the programme. It is expected that the final number of PMs and costs per partner will be adjusted on a yearly basis during the development of the AWP and based on the performance and strategic indications.

N° Ben.	WP 1	WP 2	WP 3	WP 4	WP 5	WP 6	WP 7	WP 8	WP 9	WP10	WP11	WP12	WP13	WP14	WP15	WP16	WP17	WP18	WP19	WP20	WP21	WP22	WP23	WP24	WP25	TOTAL PM
1	**90**					46	1,2		2				**8,62**			28,8			4		3,86		**4**			188,48
1.1						2	6								14,5											22,5
2	**12**	**24**																							6	42
3	1		**14,75**	**1**																						16,75
4	1		**3,25**		0,4																					4,65
5			0,75	**1,6**							**12**										3,56					17,91
6			0,75		**1,25**																					2
7	1		1,45		**2**																		4	2,58	**3**	14,03
8						**27**	18	4,5	9	8		12								2						80,5
9						**15**														0,5			4			19,5
10						24	**27**							1,5	**13,5**	9				6,9						81,9
11						3	**33**	**33**	12				5,2	5						2,5		3				96,7
12						3		**21**												0,5						24,5
13									**50**	**21**	9	12									0,97					92,97
14									**24**					9												33
15									9	**21**							6				4,38					40,38

N° Ben.	WP 1	WP 2	WP 3	WP 4	WP 5	WP 6	WP 7	WP 8	WP 9	WP 10	WP 11	WP 12	WP 13	WP 14	WP 15	WP 16	WP 17	WP 18	WP 19	WP 20	WP 21	WP 22	WP 23	WP 24	WP 25	TOTAL PM
16						3			9			**6**	10,39	**8**		2				0,5						38,89
17													**13,28**	3						0,5						16,78
18									4	9			10,71	**9**	8,25											40,96
19						9,6		3					10,71	3	**26**					0,5						52,81
20	1												6,14	5		**10**				0,5					0,4	23,04
21																**12**										12
22																	**11**	**14**		3		12				40
23	12				0,5												**3**	**20**								35,5
24						3			18	9									**12**							42
25																			**12**	1						13
26	4		1		0,2						9									**21,4**				6,43	0,4	42,43
27	1					3		6												**14**			4	9,2		37,2
28																					**19,08**					19,08
29			1,75		0,5															2		**12**		2,14	30	48,39
30	2,8																					12				14,8
31																							**8**			8
32	1																							**9,87**	0,4	11,27
33																								**8,4**		8,4
34	1,8																								**4**	5,8
35																				1						1
36													6,25	3												9,25
37																3										3
38						3																				3
39																				7					3,4	10,4

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N° Ben.	WP 1	WP 2	WP 3	WP 4	WP 5	WP 6	WP 7	WP 8	WP 9	WP 10	WP 11	WP 12	WP 13	WP 14	WP 15	WP 16	WP 17	WP 18	WP 19	WP 20	WP 21	WP 22	WP 23	WP 24	WP 25	TOTAL PM
40																										0
41			0																							0
42						3		6															4			13
43						2,4	3,6																			6
44																				17,7						17,7
45																				6,5						6,5
46						3																				3
47	18																									18
48						3																				3
49	6		0,75		0,2																					6,95
50	6										3													3,3		12,3
51									8					4						2						14
52																										0
53						3			5	2																10
54			0,75																							0,75
55																				20,6						20,6
56			0,75																							0,75
57																				1,5						1,5
58			0,75																							0,75
59			0,75																							0,75
60																				7,7						7,7
61			0,75																							0,75
62																										0
62-1			0,75																							0,75
63																				17,9						17,9
64																								3,14		3,14

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

N° Ben.	WP 1	WP 2	WP 3	WP 4	WP 5	WP 6	WP 7	WP 8	WP 9	WP1 0	WP1 1	WP1 2	WP1 3	WP1 4	WP1 5	WP1 6	WP1 7	WP1 8	WP1 9	WP2 0	WP2 1	WP2 2	WP2 3	WP2 4	WP2 5	TOTAL PM
65						2																				2
66													3,73													3,73
67			0,75	0																			4	2,58		7,33
68						3														4,2			4	5,3		16,5
69			0,75																							0,75
70															4,5					1	6,5					12
71						3																				3
72			1,2				6													1		6	4		0,4	18,6
73																							4			4
74																									1	1
75														0,6						3						3,6
76			0,75																							0,75
77						3	1,2														12,29					16,49
78			0,75																							0,75
79																9										9
80						3																				3
81						3		6															4			13
82			0,75																							0,75
83			0,75																							0,75
84						3																				3
85																							**4**			4
86																							3			3
87						6																				6
88						3																				3
89																					14,31					14,31
90																										0

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

N° Ben.	WP 1	WP 2	WP 3	WP 4	WP 5	WP 6	WP 7	WP 8	WP 9	WP 10	WP 11	WP 12	WP 13	WP 14	WP 15	WP 16	WP 17	WP 18	WP 19	WP 20	WP 21	WP 22	WP 23	WP 24	WP 25	TOTAL PM
91			0,75																							0,75
92			0,75																							0,75
93						3																		6,59		9,59
94			0,75																					2,58		3,33
95						3																				3
96																				0,5				0,71		1,21
97									10																	10
98			0,75																							0,75
99																			1,8	6,9						8,7
100			0,75																							0,75
101			0,75																							0,75
102																9										9
103			0,75																							0,75
104			0,75																							0,75
105																				2						2
106	28																									28
107																							4			4
108			0,75																					2,58		3,33
109			0,95																							0,95
110																					6,64					6,64
111																				1				3,14		4,14
112																				5,2						5,2
113																					8,94					8,94
114																			4							4
115									8												2,62					10,62
116						3																				3

N° Ben.	WP 1	WP 2	WP 3	WP 4	WP 5	WP 6	WP 7	WP 8	WP 9	WP 10	WP 11	WP 12	WP 13	WP 14	WP 15	WP 16	WP 17	WP 18	WP 19	WP 20	WP 21	WP 22	WP 23	WP 24	WP 25	TOTAL PM
117						3																				3
118						3																				3
119						3																				3
120	1,8		0,2	1	0,2															3						6,2
121							6								7,25				4							17,25
122																				3,4						3,4
123																								2,14	0,4	2,54
124																					6,62					6,62
125						3															5,98					8,98
126			0,75																							0,75
127																				1,5						1,5
128						3																				3
129			0,75																							0,75
130						3																				3
131																								0,71		0,71
132													2,82													2,82
133						3																				3
134																		4,2								4,2
135	1,8																									1,8
136																										0
136-1									5	2																7
137	15																									15
138			0,75																							0,75
139			0,75																							0,75
140																					12,08					12,08
141																			4		5,1					9,1

N° Ben.	WP 1	WP 2	WP 3	WP 4	WP 5	WP 6	WP 7	WP 8	WP 9	WP1 0	WP1 1	WP1 2	WP1 3	WP1 4	WP1 5	WP1 6	WP1 7	WP1 8	WP1 9	WP2 0	WP2 1	WP2 2	WP2 3	WP2 4	WP2 5	TOTAL PM
142																				0,5					0,4	0,9
143						3																				3
144			0,75																							0,75
145						5								1												6
146																										0
147						3																				3
148						3																				3
149						3																				3
150																									2,4	2,4
151																		*2*			*8,8*					10,8
152																									*0*	0
153			*0*																						*0*	0
154			*0*																							0
155																		*2,4*			*6*					8,4
156			*0*																							0
157																		*2,5*			*3,57*					6,07
158																		*1,3*			*1,92*					3,22
159																							*0*			0
160																		*2,4*			*17*					19,4
161													*0,33*					*1*			*3,8*					5,13
162																									*0*	0
163																					*17,47*					17,47
164																		*3,1*			*4,62*					7,72
165													*0,33*					*1*			*4,8*					6,13
166			*0*																							0
167																		*1*			*7,2*					8,2

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N° Ben.	WP 1	WP 2	WP 3	WP 4	WP 5	WP 6	WP 7	WP 8	WP 9	WP1 0	WP1 1	WP1 2	WP1 3	WP1 4	WP1 5	WP1 6	WP1 7	WP1 8	WP1 9	WP2 0	WP2 1	WP2 2	WP2 3	WP2 4	WP2 5	TOTAL PM
168																				*1*						1
169	*1,8*				*0,2*															*1,2*						3,2
170						*3*	*6*																*12*			21
171																										0
172													*1,43*		*5,5*											6,93
173				*0,6*																						0,6
174						*3*																				3
175						*3*																				3
Total	**207**	**24**	**46,3**	**4,2**	**5,45**	**241**	**108**	**79,5**	**173**	**72**	**33**	**30**	**79,94**	**52,1**	**79,5**	**82,8**	**20**	**54,9**	**41,8**	**102,7**	**258,51**	**45**	**71**	**71,39**	**52,2**	**2035,29**

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2.1.2. Other major costs table

Table 2.3.e: 'Purchase costs' items for the three years and for Year 1 (travel and subsistence, equipment and other goods, works and services)

The table of *Purchase costs* summarizes the budgets for year 1. The table below shows for each participant if the purchase costs (i.e. the sum of the costs for 'travel and subsistence', 'equipment', and 'other goods, works and services') exceeds 15% of the personnel costs for that participant, detailing cost items up to the level that the remaining costs are below 15% of personnel costs.

1/INSERM	Cost (€)	Justification
Travel and subsistence	80 700	WP1: travel to consortium meetings (1 pax per partner/1000€ per travel) (1000€); CENTRAL BUDGET - to be attributed - travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (15000€); WP23: U974 - Travel costs/accommodation costs for the NMG meetings ; CENTRAL BUDGET - To be attributed -Travel costs/accommodation costs for the Annual workshop NMG; Travel costs/accommodation WP meetings and workshop organisation; Participation on scientific conferences for dissemination purposes; WP25: Strategic Alliances - RDP mission and representation (5000€);
Other goods, works and services	534 457	CENTRAL BUDGET - To be attributed - consortium meeting (50000€)WP1; CENTRAL BUDGET - To be attributed - Budget for Multistakeholder board (25000€) WP1; CENTRAL BUDGET - To be attributed - JTC Monitoring meetings (25000€) WP3; Future MAB thematic groups WP1; Data management tools & other licences ; consumables (T21.1) (T21.2) consumables for understanding of current LNPs/EVs/NPs in T21.3.1, the evaluation of efficacy on T21.3.3, demonstration of scalability in T21.3.4 consumables - rodent models to mimic adaptive immune response (T21.5.2) and Cas9 immunogenicity in rodent models (T21.5.4) ; CENTRAL BUDGET - To be attributed -Publication costs WP23 ; CENTRAL BUDGET - to be attributed - Use case incentives for underrepresented countries (long-read genomics tests) ; Inserm ART-ARNm - consumables and models (rodents, organoids..) for PoC studies (T3) ; publication fees WP11
Remaining purchase costs (<15% of pers. Costs)	3 000	
TOTAL	**618 157**	
2/TEAMIT	Cost (€)	Justification
Other goods, works and services	122 900	WP2.3. All the communication materials and tools such as videos, infographics, animated infographics, design, website back-end programming and maintenance, podcast, outsourcing engagement events
Remaining purchase costs	1 000	
TOTAL	**123 900**	
3/DLR	Cost (€)	Justification
Travel and subsistence	4 700	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ; WP4: travel costs of partners for WP4 meetings)
Other goods, works and services	87 628	WP3.2.2 2 Evaluation meetings JTC2025 (40K€ per meeting) (80000€) WP3; Reimbursement of patient experts (3 experts, 400 € per meeting, 1 meeting) (1200€) WP3; Reimbursement of ethics experts (3 experts per proposal, 100 € per review, 21 proposals) (6428€) WP3
TOTAL	**92 328**	
4/ANR	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;

TOTAL	**3 220**	
5/FTELE	Cost (€)	Justification
Travel and subsistence	4 700	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ; WP4: travel costs of partners for WP4 meetings
Remaining purchase costs	700	
TOTAL	**5 400**	
6/LMT	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
8/UT	Cost (€)	Justification
Travel and subsistence	11 867	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP20.3.1: travels and accommodation for 8 trainers/staff for 2-3 days /year + 2 fellowships/year WP6: Workshop to prepare, facilitate and instigate diagnostic research data collation and federation WP9: T3 - 2 meeting travels/yr T5 - 2 travels/yr
Other goods, works and services	107 624	Task 20.3.1. Catering costs: 30 people, 2 to 3-day meeting / year ; Case study 1 ; WP10: T1 Longitudinal validation studies PROM ;
TOTAL	**119 491**	
13/UKHD	Cost (€)	Justification
Travel and subsistence	23 000	WP1: travel to 1 consortium meeting and WP meetings (1000€) WP9: T2 - 2 meeting travels/yr for 4 years (6 travels in Y1 to 3) T3 - 1 workshop + 12 travels T4 - 4 travels/yr T5 - 2 travels/yr T6 - 6 travels
Other goods, works and services	199 540	WP9: RESERVE POT - to be allocated - T3 - financial support to external partners (cohort data provision) ; RESERVE POT - to be allocated - T6 - financial support to external partners (provision of additional data to improve cohort quality) ; WP10: RS - Longitudinal validation studies PROM (T1) ; RS - Meetings (T1) - 2 meetings per use case ; RS - T1 PAO reimbursement (10.000€ per year per use case)); WP11: Workshops (T1/multistakeholder); WP12: IT infrastructure registry for N-of-1 treatment capture ; Case study 2 WP21: Consumables for T21.1 (Establishment of a rAAV base manufacturing process in suspension cells) ;
TOTAL	**222 540**	
15/VHIR	Cost (€)	Justification
Other goods, works and services	120 206	WP10: T1 Longitudinal validation studies PROM ; Meetings (T1) - 2 meetings per use case ; PAO reimbursement ; mHealth adaptation or new creation; T2 - Design meeting ; WP21: consumables for Comparison and characterization of PK and biodistribution of mRNA formulations upon various routes of administration (i.v, i.m, i.p, i.n) (T21.3.5); Laboratory reagents and consumables for testing different vectors (T21.1.1) and for validation assays and inter-lab variability assays T21.1.2)
Remaining purchase costs	3 000	
TOTAL	**123 206**	
16/LUMC	Cost (€)	Justification

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Travel and subsistence	45 720	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP12 organisation of meetings, WP14 organisation workshop;
Other goods, works and services	11 467	WP12 consumables toxicity technician ; WP14: 1xBYOD hackathon (meeting organisation - room, catering , etc) 4400
TOTAL	**57 187**	
22/EATRIS	Cost (€)	Justification
Travel and subsistence	20 018	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP17: In-person WP meeting (8 participants, 2 delegates per partner WP18: Meeting of RDP Regulatory Support Group (including NCA members + EMA representatives) M12 (14800€) WP20.3.2: travels and accommodation for 8 trainers/staff for 2-3 days /year + 2 fellowships/year
Other goods, works and services	61 446	WP18 IT and web design support for upgrading of the Regulatory Information System (13333); WP17: IT and web design support for Innovation Management Toolbox updates (3600); task 20.3.2. Catering costs: 30 people, 2 to 3-day meeting / year (3180€); WP22: Share of Global Data subscription (8000€) ; Nonclinical validation steps for selected projects (2 projects @50k each) (33333€)
TOTAL	**81 464**	
24/APHP	Cost (€)	Justification
Travel and subsistence	16 250	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP9: T1 - 4 meeting travels/yr T2 - 2 meeting travels/yr T3 - 2 meeting travels/yr (4000€) WP19 yearly WP meetings (11250)
Other goods, works and services	68 861	WP19 publication fees (750€) WP10 T1 Longitudinal validation studies PROM ; Meetings (T1) - 2 meetings per use case ; T1 PAO reimbursement (10.000€ per year per use case) (68111€)
TOTAL	**85 111**	
26/EURORDIS	Cost (€)	Justification
Travel and subsistence	90 700	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); Task 20.1 accommodation and travels for 25 trainers + accommodation for 70 trainees + 12 travel fellowships / year (89700€)
Other goods, works and services	47 932	WP3: Patient working group meetings (1 meeting) (6666€); Task 20.1.1. Catering costs + room (34600€); WP11 Workshops (T1/multistakeholder) (6666€);
TOTAL	**138 632**	
27/VULSK	Cost (€)	Justification
Travel and subsistence	18 960	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); Task 24.1 - Knowledges exchanges - 4 meetings Y1 (15000€) WP23: Travel costs/accommodation costs for the Annual workshop; Travel costs/accommodation costs for the Annual general meeting (2960€)
Remaining purchase costs	2 830	
TOTAL	**21 790**	
28/UC	Cost (€)	Justification

Other goods, works and services	75 762	WP21: T21.1; Tissue/cell-specific expression (e.g., brain, liver, immune cells) and CRISPR-Cas9 model system for sequence standardization (T21.2.1); demonstration of efficacy in vitro head-to-head comparison of RNA molecules (T21.2.4); consumables for understanding of current LNPs/EVs/NPs in T21.3.1, the evaluation of efficacy on T21.3.3, demonstration of scalability in T21.3.4; deliver editing tools in mouse model of SCA3 (T21.4.2); in vivo work in SCA3 mouse model; 6,000€ for in vitro editing in iPS derived neural cells (T21.4.1); rodent models to mimic adaptive immune response (T21.5.2)
Remaining purchase costs	1 000	
TOTAL	**76 762**	
29/FFRD	Cost (€)	Justification
Travel and subsistence	10 887	WP1 travel to 1 consortium meetings (1 pax per partner/1000€ per travel)(1000€); JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) WP1; Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) WP3; IRDiRC mission and representation WP25
Other goods, works and services	105 130	WP25: IRDiRC - One in person CA-SC meeting per year (75K) ; ; Task Force workshop (20k€/year) WP22: Host matchmaking, review and monitoring meetings (3 meetings lunch-to-lunch at €10,130 per meeting of 10 people) 10130€
TOTAL	**116 017**	
31/CCUH	Cost (€)	Justification
Travel and subsistence	9 140	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); organisation workshop; WP23: Travel costs/accommodation costs for the Annual workshop; Travel costs/accommodation costs for the Annual general meeting (4440€)+ RESERVE POT (to be allocated) - Travel costs/accommodation costs for the Annual workshop from Y1 to Y3 topic experts - 5 pax per workshop (3700€)
Other goods, works and services	14 528	WP23 RESERVE POT (to be allocated) - Catering costs for the Annual 3.2 workshop
TOTAL	**23 668**	
34/RDI	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
TOTAL	**1 000**	
35/ACU	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
TOTAL	**1 000**	
39/ASU-FC	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
TOTAL	**1 000**	
40/BIU	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
Other goods, works and services	19 286	WP21 Evaluation of off-target effects ex vivo (GUIDE-Seq, rhAmpSeq) (T21.4.3)
TOTAL	**20 286**	
41/BMBF	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
TOTAL	**1 000**	

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44/CHARITE	Cost (€)	Justification
Other goods, works and services	40 828	WP21: consumables for T21.2.1; consumables for T21.2.2; consumables for in vitro and in vivo analysis in T21.2.4; consumables for T21.3; consumables for multiparameter flow cytometry (T.21.5.1); analysis of humanized NSG mice exposed to tools developed in T21.1-T21.4 (T.21.5.2), Generation of specific Treg and r PoC specific Treg in vitro and in vivo (humanized mice) (T21.5.4)); WP21 - Central budget to be allocated - Consumables T21.5 ;
Remaining purchase costs	1 000	
TOTAL	**41 828**	
45/CHI	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
Remaining purchase costs	26 857	WP21: Consumables for: multiligand assays and for multiomics single cell analyses (T.21.5.1), for analysis of humanized NSG mice exposed to tools T21.1-T21.4 (T.21.5.2), qualification of single cell platform (T.21.5.3) ;
TOTAL	**27 857**	
52/ELS	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
Other goods, works and services	111 320	WP1 Elsevier Licence ;
TOTAL	**112 320**	
53/Erasmus MC	Cost (€)	Justification
Travel and subsistence	2 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP9: T1 - 2 meeting travels/yr (1000€);
Other goods, works and services	68 111	WP10 T1 Longitudinal validation studies PROM ; meetings per case ; T1 PAO reimbursement (10.000€ per year per use case)
TOTAL	**70 111**	
54/F.R.S.-FNRS	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
55/FHG	Cost (€)	Justification
Other goods, works and services	44 195	WP21: Consumables for analytics (T21.1.1, T21.1.2); Development of an in vitro screening system to select optimal RNA constructs (T21.2.3); and consumables for large scale production of RNAs (T21.2.5); T21.3 (44195)
Remaining purchase costs	1 000	
TOTAL	**45 195**	
56/FRRB	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
57/ECRIN	Cost (€)	Justification
Travel and subsistence	3 867	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP20.3.4: travels and accommodation for 8 trainers/staff for 2-3 days /year + 2 fellowships/year

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Other goods, works and services	1 060	task 20.3.4. Catering costs
TOTAL	**4 927**	
58/FWF	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
59/ IFD	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
61/FCT	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
62.1 AZV	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
63/GNT	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
Other goods, works and services	36 738	WP21: consumables and reagents for viral vector production and characterization (T21.1.1) and for QC testing (T21.1.2); Analytical characterization and screening of optimal RNA molecules (T21.2.3) and Proof of principle demonstration of efficacy in vitro and head-to-head comparison of selected RNA molecules (T21.2.4); in vitro editing of DMD myoblasts (Cas 9, base editors, molecular biology) (T21.4.1) and for in vivo editing in DMD mouse model, plus analysis of off target effect in vivo (AAV Cas9 and base editing, molecular biology and histology) (T21.4.2)
TOTAL	**37 738**	
67/HRB	Cost (€)	Justification
Travel and subsistence	6 180	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ; WP23: Travel costs/accommodation costs for the Annual workshop; Travel costs/accommodation costs for the Annual general meeting (2960€)
TOTAL	**6 180**	
69/Rannis	Cost (€)	Justification

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Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
70/IMAGINE	Cost (€)	Justification
Travel and subsistence	5 278	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP meetings (training)
Other goods, works and services	14 991	task 20.1.2: catering costs for 20 people for 2 day-meeting (1 edition) ; WP21: Consumables - Molecular and cellular biology reagents (including DNA/RNA synthesis, antibodies, Tissue culture supplies and transfection reagents), mouse experiments and laboratory disposables (T21.4.1 and T21.4.2) ;
TOTAL	**20 269**	
73/INSA	Cost (€)	Justification
Travel and subsistence	3 960	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP23: Travel costs/accommodation costs for the Annual workshop; Travel costs/accommodation costs for the Annual general meeting (2960€)
TOTAL	**3 960**	
74/IOR	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
TOTAL	**1 000**	
75/ISS	Cost (€)	Justification
Travel and subsistence	13 087	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP meetings (training, workshop)
Other goods, works and services	4 647	task 20.3.5. Catering costs: 30 people, 2 to 3-day meeting / year ; WP14 1xBYOD hackathon (meeting organisation - room, catering , etc) ;
TOTAL	**17 734**	
76/IT-MOH	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
77/KU Leuven	Cost (€)	Justification
Other goods, works and services	27 993	WP21: consumables (so reagents, materials and plastics) associated to T21.1 ;
Remaining purchase costs	1 000	
TOTAL	**28 993**	
78/LZP	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
82/MUR	Cost (€)	Justification

Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
83/NCBR	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
85/MoH SR	Cost (€)	Justification
Travel and subsistence	3 960	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP23: Travel costs/accommodation costs for the Annual workshop; Travel costs/accommodation costs for the Annual general meeting (2960€)
TOTAL	**3 960**	
86/RDG	Cost (€)	Justification
Travel and subsistence	3 960	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP23: Travel costs/accommodation costs for the Annual workshop; Travel costs/accommodation costs for the Annual general meeting (2960€)
TOTAL	**3 960**	
89/OSR	Cost (€)	Justification
Other goods, works and services	105 105	WP21: mouse experiments and laboratory disposable (T.21.4.2); consumables: Molecular and cellular biology reagents (including DNA/RNA synthesis, antibodies, Tissue culture supplies and transfection reagents) (T21.4.1); mouse experiments, in vivo GE barcoding, LiBiSseq and SLIM PCR (T21.4.3); • consumables for multiparameter flow cytometry, generation of Ag-specific cell lines (T.21.5.1), Generation of specific Treg and PoC specific Treg in vitro and in vivo (humanized mice) (T21.5.4) ;
Remaining purchase costs	1 000	
TOTAL	**106 105**	
90/JSI	Cost (€)	Justification
Travel and subsistence	3 960	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP23: Travel costs/accommodation costs for the Annual workshop; Travel costs/accommodation costs for the Annual general meeting (2960€)
TOTAL	**3 960**	
91/RCN	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
92/FWO	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
93/REUH	Cost (€)	Justification

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Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
TOTAL	**1 000**	
94/RIF	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
98/SPW	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
99/SFU	Cost (€)	Justification
Travel and subsistence	3 867	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP20.3.4: travels and accommodation for 8 trainers/staff for 2-3 days /year + 2 fellowships/year 2867€
Other goods, works and services	1 810	WP19: publication fees (750€); task 20.3.4. Catering costs: 30 people, 2 to 3-day meeting / year (1060€) ;
TOTAL	**5 677**	
100/ETAg	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
101/SAS	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
103/MOSAE	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
104/SRC	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
105/TEDDY	Cost (€)	Justification

Travel and subsistence	4 727	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); task 20.1.2: travels and accommodation for 10 trainers and staff / year + 3 travel fellowships per year (1 edition) 3727€
Other goods, works and services	1 420	task 20.1.2: catering costs for 20 people for 2 day-meeting (1 edition) (4260€);
TOTAL	**6 147**	
107/TIF	Cost (€)	Justification
Travel and subsistence	3 960	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP23: Travel costs/accommodation costs for the Annual workshop; Travel costs/accommodation costs for the Annual general meeting (2960€)
TOTAL	**3 960**	
108/TUBITAK	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
109/RT (TuscReg)	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
110/UAB	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
Remaining purchase costs	6 429	WP21: Plastic ware and reagents for viral vector production and characterization (T21.1.1), Taqman qPCR reagents to quantify the vector yield in each production. Consumables for analytics (T21.1.2) ;
TOTAL	**7 429**	
112/UCSC	Cost (€)	Justification
Travel and subsistence	4 900	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP20.4 :Task 20.4 - Accommodation & Travel costs for 10 trainers 4 days Task 20.4 - Accommodation & Travel costs for 5 fellows 3900€
Other goods, works and services	4 067	WP20.4 Task 20.4. catering costs for speakers (10) Task 20.4. classrooms and wrap meeting costs
TOTAL	**8 967**	
113/UEF	Cost (€)	Justification
Other goods, works and services	17 600	WP21: consumables (T21.2.1), consumables (T21.2.2), consumables for in vitro and in vivo (T21.2.4); consumables for T21.3 ;
Remaining purchase costs	1 000	
TOTAL	**18 600**	
115/UKLFR	Cost (€)	Justification
Travel and subsistence	2 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP9: T5 - 2 travels/yr (1000€)
Other goods, works and services	22 857	WP21: Evaluation of off-target effects in vivo (CAST-Seq, rhAmpSeq, long-read seq) (T21.4.3); • for Evaluation of off-target effects ex vivo (CAST-Seq, rhAmpSeq, long-read seq) (T21.4.3) ;
TOTAL	**24 857**	

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122/c4c-S	Cost (€)	Justification
Travel and subsistence	12 180	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); task 20.1.2: travels and accommodation for 10 trainers and staff / year + 3 travel fellowships per year (1 edition) 11180€
Other goods, works and services	4 260	WP20.1.2: catering costs for 20 people for 2 day-meeting (1 edition);
TOTAL	**16 440**	
124/CNRS	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
Other goods, works and services	12 571	WP21: For consumables for understanding of current LNPs/EVs/NPs in T.21.3.1, evaluation of efficacy T.21.3.3, AI tools development (T.21.3.2), demonstration of scalability in T.21.3.4, and regulatory challenges with EV and biohybrids encapsulating mRNA (T21.3.6) ;
TOTAL	**13 571**	
125/CIBER	Cost (€)	Justification
Other goods, works and services	27 323	WP21: consumables for targeting to hematopoietic stem cells, PBMC subsets, CNS and liver (T21.3.1), and in vitro and in vivo evaluation of efficacy, immunogenicity and safety of mRNA formulations (T21.3.3); • for mouse experiments and laboratory disposables (T21.4.2), for consumables: Molecular and cellular biology reagents (including DNA/RNA synthesis, antibodies, Tissue culture supplies and transfection reagents) (T21.4.1);
Remaining purchase costs	1 000	
TOTAL	**28 323**	
126/UEFISCDI	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3: Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
129/BNSF	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3: Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
136.1/KUM	Cost (€)	Justification
Travel and subsistence	10 167	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP9: T1 - 2 meeting travels/yr T4 - Kick-off workshop, 3 travels to EMA, 6 travels for project (9167€)
Other goods, works and services	68 111	WP10: T1 Longitudinal validation studies PROM ; Meetings (T1) - 2 meetings per use case ; T1 PAO reimbursement (10.000€ per year per use case)
TOTAL	**78 278**	
138/FNR	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
139/NKFIH	Cost (€)	Justification

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Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
140/PEI	Cost (€)	Justification
Other goods, works and services	12 568	WP21 Consumables for setting up and validating quality assays on AAV vector stocks (Task 21.1); Consumables for T21.2; Consumables for T21.3;
Remaining purchase costs	1 000	
TOTAL	**13 568**	
141/PLUS	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
Other goods, works and services	18 083	WP21 For understanding of current LNPs/EVs/NPs in T21.3.1; WP19: PUBLICATION FEE (750€)
TOTAL	**19 083**	
142/SU	Cost (€)	Justification
Travel and subsistence	1 000	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€);
TOTAL	**1 000**	
144/Vinnova	Cost (€)	Justification
Travel and subsistence	3 220	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP1: JTC CSC travel to monitoring meetings (1 meetings x740€) (740€) ; WP3:Travel costs to 2 evaluation meetings at average budget of 740 € (500 Travel+240 Hotel 2 nights) (1480€) ;
TOTAL	**3 220**	
149/UO	Cost (€)	Justification
Travel and subsistence	3 960	WP1: travel to 1 consortium meetings (1 pax per partner/1000€ per travel) (1000€); WP23: Travel costs/accommodation costs for the Annual workshop; Travel costs/accommodation costs for the Annual general meeting (2960€)
TOTAL	**3 960**	

3. Annex 1 - List of Abbreviations

Acronym	Full name	Acronym	Full name
1+MG	1+ Million Genome initiative	C&D	Communication and Dissemination
1M1M	1 mutation 1 medicine (initiative)	CA	Consortium Agreement
AAV	Adeno-Associated Virus	CDA	Confidential Disclosure Agreement
ACT EU	Accelerating Clinical Trials in the European Union	CDISC	Clinical Data Interchange Standards Consortium
ADPKD	Autosomal Dominant Polycystic Kidney Disease	CDM	Common Data Model
AI	Artificial Intelligence	cDNA	complementary DNA
AIM-IMA	Agence InterMutualiste	CHMP	Committee for Medicinal Products for Human Use
API	Application Programming Interface	CITEseq	Cellular Indexing of Transcriptomes and Epitopes by Sequencing
ARCA	Autosomal Recessive Cerebellar Ataxia	ClinRO	Clinician-Reported Outcome
ASO	Antisense Oligonucleotides	CNV	Copy Number Variation
ASTERIX	Advances in Small Trials dEsign for Regulatory Innovation and eXcellence	COA	Clinical Outcome Assessment
ATMP	Advanced Therapy Medicinal Product	COI	Cost of Illness
AWP	Annual Work Programme	Coo	(ERDERA) Coordination (team)
AWP1	Annual Work Plan Year 1	COST	European Cooperation in Science and Technology
AWP2	Annual Work Plan Year 2	CRN	Clinical Research Network
AXD	Alexander Disease	CS	Clinical Studies
B1MG	Beyond 1 Million Genomes	CSC	Call Steering Committee
BGTC	Bespoke Gene Therapy Consortium	CT	Clinical Trial
BM	Business Model	CTEB	Clinical Trial Evaluation Board
BMC	Business Model Canvas	CTO	Chief Technology Officer
BNDMR	French National Rare Disease Registry	CTSC	Clinical Trial Scientific Committee
BoD	Burden Of Diseases	CWL	Common Workflow Language
BoF	Board of Funders	D	Deliverable
BSEP	Bile Salt Export Pump	DALY	Disability-Adjusted Life Years
BYOD	Bring Your Own Data	DARWIN	Data Analysis and Real World Interrogation Network

Acronym	Full name	Acronym	Full name
DATF	Data Analysis Task Force	EHR4CR	Electronic Health Records for Clinical Research
DDD	Dense Deposit Disease	EJP RD	European Joint Programme on Rare Diseases
DDT	Drug Development Tools	ELISA	enzyme-linked immunosorbent assay
DG CONNECT	Directorate-General for Communications Networks, Content and Technology	ELSA	Ethical, Legal and Social Aspects
DG JRC	Directorate-General Joint Research Center	ELSI	Ethical, Legal, and Social Issues
DG RTD	Directorate-General for Research and Innovation	EMA	European Medicines Agency
DG SANTE	Directorate-General for Health and Food Safety	EO	Expected Outcome
DH	Data Hub	EOSC	European Open Science Cloud
DITF	Data Interpretation Task Force	ePAGs	European Patient Advocacy Groups
DMD	Duchenne Muscular Dystrophy	EPAs	Entrustable Professional Activities
DMP	Data Management Plan	ERA4Health	Fostering a European Research Area for Health Research
DNA	Deoxyribonucleic Acid	ERC	European Research Council
DSB	DNA Double-Strand Break	ERDERA	European Rare DisEases Research Alliance
DSH	Data Services Hub	ERICA	The European Rare Disease Research Coordination and Support Action consortium
DSW	Data Stewardship Wizard	ERKNet	European Reference Network on kidney diseases
EAG	Ethics Advisory Group	ERKReg	The European Rare Kidney Disease Registry
EATRIS	European infrastructure for translational medicine	ERN	European Reference Network
EBI	European Bioinformatics Institute	ERN CRANIO	ERN on craniofacial anomalies and ear, nose and throat (ENT) disorders
EC	European Commission	ERN GENTURIS	ERN on genetic tumour risk syndromes
ECRIN	European Clinical Research Infrastructure Network	ERN-EpiCARE	ERN on epilepsies
ECTS	European Credit Transfer and Accumulation System	ERN-ERNICA	ERN for rare Inherited and Congenital Anomalies
EFPIA	European Federation of Pharmaceutical Industries Associations	ERN-EuroBloodNet	ERN on haematological diseases
EGA	European Genome-Phenome Archive	ERN-ITHACA	European Reference Network on congenital malformations and rare intellectual disability
EHDS	European Health Data Space	ERN-RDN	ERN on neurological diseases
EHR	Electronic Health Record	ERN-RITA	ERN on immunodeficiency, autoinflammatory and autoimmune diseases

Acronym	Full name	Acronym	Full name
ESFRI	European Strategy Forum on Research Infrastructures	GPAP	Genome Phenome Analusis Platform
ESHG	European Society of Human Genetics	HCP	Health Care Practitioner
EU	European Union	HDR	Homology Directed Repair
EUCOPE	European Confederation of Pharmaceutical Entrepreneurs	HER	Health Electronic Record
EUHA	European University Hospital Alliance	HGVS	Human Genome Variation Society
EuReCA	EU Resource Efficiency Coordination Action	HITI	Homology-Independent Targeted Integration
EURO-NMD	European Reference Network for Rare Neuromuscular Diseases	HOOM	HPO-ORDO Ontological Module
EVs	Extracellular Vesicles	HPO	Human Phenotype Ontology
ExCom	Executive Committee	HSPC	Hematopoietic Stem and Progenitor Cells
F2F	Face-to-Face	HTA	Health Technology Assessment
FAIR	Findable, Accessible, Interoperable, Reusable	i.p.	Intraperitoneal injection
FDA	U.S. Food and Drug Administration	ICF	International Classification of Functioning, Disability and Health
FHIR	Fast Healthcare Interoperability Resource	ICT	Innovative Cellular Therapeutics
FP	Framework Programme	IDEAL	Integrated DEsign and AnaLysis of clinical trials in small population group
GA4GH	Global Alliance for Genomic Health	IEA	Independent Ethics Advisor
GB	Governing Board	IHI	Innovative Health Initiative
GCLP	Good clinical laboratory practice	IMT	Innovation Management Toolbox
GCP	Good Clinical Practice	InSPiRe	Innovative methodology for small populations research
GDI	Genomic Data Infrastructure	IP	Intellectual Property
GDPR	General Data Protection Regulation	IPR	Intellectual Property Rights
GenoMed4All	Genomics and Personalized Medicine for all	iPSC	induced Pluripotent Stem Cells
GMP	Good Manufacturing Practice	IRDiRC	International Rare Diseases Research Consortium
GMS	Genomic Medicine Sweden	ISA	Investigation, Study and Assay
GO	General Objective	IT	Information Technology
GoF	Gain of Function	ITR	Inverted Terminal Repeat sequences

Acronym	Full name	Acronym	Full name
IV	Intravenous	NGO	Non-Governmental Organization
JARDIN	Joint Action for Integration of ERNs	NGS	Next Generation Sequencing
JCS	Joint Call Secretariat	NHEJ	Non-Homologous End Joined
JRC	Joint Research Centre	NIH	National Institutes of Health
JTC	Joint Transnational Call	NLP	Natural Language Processing
KPI	Key Performance Indicator	NMG	National Mirror Group
LNP	Lipid Nanoparticles	NP	National Plan
LOINC	The international standard for identifying health measurements, observations, and documents	NSHS	National System of Health Data
LRS	Long-Read Sequencing	NSS	Networking Support Scheme
LS AAI	Life Science Authentication and Authorization Infrastructure	NTP	National Training Provider
M	Month	OA	EURORDIS Open Academy
MAB	Multistakeholder Advisory Board	ObsRO	Observer Reported Outcome
MAxO	Medical Action Ontology	ODD	Orphan Drug Designation
MEI	Mobile Element Insertions	OFCO	Orphanet Functional Consequences Ontology
metabERN	European Reference Network on hereditary metabolic disorders	OG	Operating Group
mHEALTH	Mobile health solutions	OGM	Optical Genome Mapping
MHLW	Japanese Ministry of Health, Labour and Welfare	OMIM	Online Mendelian Inheritance in Man
ML	Machine Learning	OMOP	Observational medical outcomes partnership
MoU	Memoranda of Understanding	OMP	Orhan Medicinal Product
MRI	Magnetic Resonance Imaging	OO	Operational Objective
mRNA	Messenger Ribonucleic Acid	ORDO	Orphanet Rare Disease Ontology
MS	Member States	p-medicine	Personalised Patient Information for Clinical Decision Support
mtDNA	Mitochondrial Deoxyribonucleic Acid	PAES	Post-Authorization Efficacy Studies
NAB	National Alignment Board	PAO	Patient Advocacy Organization
NBS	Newborn Screening	PASS	Post-Authorization Safety Surveillance

Acronym	Full name	Acronym	Full name
PBMC	Peripheral Blood Mononuclear Cells	SAWP	Scientific Advice Working Party
PCR	Polymerase Chain Reaction	SB	Sleeping Beauty
PerfO	Performance Outcomes	SC	Steering Committee
PLWRD	People Living With a Rare Disease	sc-RNA	Single Cell RNA
PMDA	Japanese Pharmaceuticals and Medical Devices Agency	SCD	Sickle Cell Disease
PPIE	Patient and Public Involvement and Engagement	SciSec	IRDiRC Scientific Secretariat
PREMs	Patient-Reported Experience Measures	scRNA-seq	Single Cell RNA sequencing
PRO	Patient Reported Outcome	SEC	Scientific Evaluation Committee
PROMs	Patient Reported Outcome Measures	SMA	Spinal Muscular Atrophy
QC	Quality Control	SME	Small and Medium Enterprise
QoL	Quality of Life	SNP	Single-Nucleotide Polymorphism
QSAR	Quality Structure Activity Relationship	SO	Specific Objective
R&I	Research and Innovation	SOA	Service-Oriented Architecture
rAAV	recombinant Adeno-Associated Virus	Solve-RD	Solving the Unsolved Rare Diseases
RADeep	Rare Anaemia Disorders European Epidemiological platform	SOP	Standard Operating Procedure
RD	Rare Disease(s)	SPAX	Spastic Ataxia Diseases
RDCA-DAP	The C-Path Rare Disease Cures Accelerator-Data and Analytics Platform	SPE	Secure Processing Environment
REAL	Re-Analysis Logistics	SRIA	Strategic Research and Innovation Agenda
RESTORE	Large Scale Research Initiative in Europe	SSSOM	Simple Standard for Sharing Ontological Mappings
RNA	Ribonucleic Acid	ST	Sub-Task
RNA-seq	RNA sequencing	STL	Sub-Task Leader
RRI	Responsible Research and Innovation	STR	Short Tandem Repeat
RSG	Regulatory Support Group	SV	Structural Variant
RWD	Real World Data	SWOT	strengths, weaknesses, opportunities, threats
RWE	Real World Evidence	T	Task

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Acronym	Full name
T2T	Telomer-to-Telomer
TCRseq	T Cell Receptor Sequencing
TF	Task Force
TL	Task Leader
TRANSFoRm	Translational Research and Patient Safety in Europe
TRE	Trusted Research Environments
UC	Underrepresented Countries
UDN	Undiagnosed Disease Networks
UDP	Undiagnosed Rare Disease Programs
UI	User Interface
USA	United States of America
UX	User Experience
VLPs	Virus-Like Particles
VP	Virtual Platform
VUS	Variant of Unknown Significance
WG	Working Group
WHO	World Health Organization
WP	Work Package
WS	Work Stream
YPAG	Young Persons Advisory Group

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4. **Annex 2 - Letter of support to ERDERA** from the European Confederation of Pharmaceutical Entrepreneurs (**EUCOPE**), the European Federation of Pharmaceutical Industries and Associations (**EFPIA**), and the EuropaBio Association of Bioindustries (**EuropaBio**)







Daria Julkowska
Assistant Director IT GGB
INSERM
8 rue de la Croix Jarry
75013 Paris, France

Ref.: MCH/68.023

Brussels, 15 September 2023

Dear Dr Julkowska,

The European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), the European Federation of Pharmaceutical Industries and Associations (EFPIA), and the EuropaBio Association of Bioindustries (EuropaBio), are very pleased to express their strong support to the upcoming European Rare Disease Partnership, now called ERDERA (**E**uropean **R**are **D**iseas**e**s **R**esearch **A**lliance).

The objectives of ERDERA are indeed very well aligned with the Rare Disease Moonshot vision - i.e. enabling and accelerating research and development across rare diseases white spots - to which our three organisations are fully committed as demonstrated by our and our members' participation in ongoing and future European and international initiatives including engagement with EJPRD amongst others.

We see ERDERA as an important step to strengthen the European translational research ecosystem and to make Europe more attractive for the most difficult areas of research, by defragmenting communities and activities, aligning agendas and stakeholders and building on or deploying infrastructures and capabilities that will help to close the gap between academic and industrial research, including regulatory readiness and technological maturity.

We firmly believe that ERDERA will remain a partner of choice for implementing the RD Moonshot recommendations for public private collaborations to ensure that Europe benefits from the cutting-edge medical science, responds quickly to patients' needs and remains a global leader in biopharmaceutical innovation for rare and paediatric diseases.

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EFPIA, EUCOPE and EuropaBio wish to continue the dialogue with EJPRD and ERDERA and evaluate whether and how we could partner in the future beyond the commitments already made by our member companies.

Yours sincerely,



Magda Chlebus, Executive Director, Science Policy & Regulatory, EFPIA



Alexander Natz, Secretary-General, EUCOPE



Claire Skentelberry, Director General, EuropaBio

About EFPIA: The European Federation of Pharmaceutical Industries and Associations (EFPIA) represents the biopharmaceutical industry operating in Europe. Through its direct membership of 37 national associations, 40 leading pharmaceutical companies and a growing number of small and medium-sized enterprises (SMEs), EFPIA's mission is to create a collaborative environment that enables our members to innovate, discover, develop and deliver new therapies and vaccines for people across Europe, as well as contribute to the European economy.

About EUCOPE: The European Confederation of Pharmaceutical Entrepreneurs (EUCOPE) is Europe's trade body that gives a bigger voice to small and mid-sized innovative companies working in the field of biopharmaceuticals and medical technologies. Through its members, EUCOPE represents 2600+ health technology companies that are researching, developing, supplying, manufacturing, and deploying the next generation of pharmaceutical innovation and therapeutic solutions around the continent. www.eucope.org

About EuropaBio: EuropaBio, the European Association for Bioindustries, promotes an innovative and dynamic European biotechnology industry. EuropaBio and its members are committed to the socially responsible use of biotechnology to improve quality of life, to prevent, diagnose, treat and cure diseases, to improve the quality and quantity of food and feedstuffs and to move towards a biobased and zero-waste economy.

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ANNEX 2

ESTIMATED BUDGET FOR THE ACTION

	Estimated eligible[1] costs (per budget category)											Estimated EU contribution[2]			
	Direct costs									Indirect costs	Total costs	EU contribution to eligible costs			Maximum grant amount[6]
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories		E. Indirect costs[3]		Funding rate %[4]	Maximum EU contribution[5]	Requested EU contribution	
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	D.1 Financial support to third parties	D.2 Internally invoiced goods and services	E. Indirect costs					
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[7]	Actual costs	Actual costs	Actual costs	Actual costs	Actual costs	Unit costs (usual accounting practices)	Flat-rate costs[8]					
	a1	a2	a3	b	c1	c2	c3	d1	d2	e = 0,25 * (a1 + a2 + a3 + c1 + c2 + c3)	f = a+b+c+d+e	U	g = f * U%	h	m
1 - INSERM	5 053 040.00	0.00	0.00	117 857.00	207 580.00	9 000.00	1 853 987.00	0.00	10 286.00	1 780 901.75	9 032 651.75	50	4 516 325.88	4 516 325.88	4 516 325.88
1.1 - CAD	572 800.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	143 200.00	716 000.00	50	358 000.00	358 000.00	358 000.00
2 - TEAMIT	819 000.00	0.00	0.00	0.00	3 000.00	0.00	372 700.00	0.00	0.00	298 675.00	1 493 375.00	50	746 687.50	746 687.50	746 687.50
3 - DLR	338 253.00	0.00	0.00	0.00	13 360.00	0.00	91 628.00	0.00	0.00	110 810.25	554 051.25	50	277 025.63	277 025.63	277 025.63
4 - ANR	125 007.00	0.00	0.00	0.00	11 140.00	0.00	11 628.00	12 857 143.00	0.00	36 943.75	13 041 861.75	50	6 520 930.88	3 907 279.49	3 907 279.49
5 - FTELE	398 498.00	0.00	0.00	0.00	14 100.00	0.00	90 050.00	3 000 000.00	0.00	125 662.00	3 628 310.00	50	1 814 155.00	1 401 160.30	1 401 160.30
6 - LMT	20 125.00	0.00	0.00	0.00	9 660.00	0.00	0.00	428 571.00	0.00	7 446.25	465 802.25	50	232 901.13	152 891.05	152 891.05
7 - ZonMw	409 966.00	0.00	0.00	0.00	18 540.00	0.00	4 000.00	5 400 000.00	0.00	108 126.50	5 940 632.50	50	2 970 316.25	1 990 795.26	1 990 795.26
8 - UT	1 997 750.00	0.00	0.00	0.00	35 600.00	0.00	320 513.00	0.00	0.00	588 465.75	2 942 328.75	50	1 471 164.38	1 471 164.38	1 471 164.38
9 - UTARTU	326 622.00	0.00	0.00	0.00	29 880.00	0.00	4 000.00	0.00	0.00	90 125.50	450 627.50	50	225 313.75	225 313.75	225 313.75
10 - CNAG	1 476 548.57	0.00	0.00	0.00	76 960.00	0.00	16 720.00	0.00	0.00	392 557.14	1 962 785.71	50	981 392.86	981 392.86	981 392.86
11 - SRUMC	2 401 800.00	0.00	0.00	0.00	51 460.00	0.00	77 180.00	0.00	0.00	632 610.00	3 163 050.00	50	1 581 525.00	1 581 525.00	1 581 525.00
12 - TUM	539 500.00	0.00	0.00	0.00	3 000.00	0.00	4 000.00	0.00	0.00	136 625.00	683 125.00	50	341 562.50	341 562.50	341 562.50
13 - UKHD	1 873 670.00	0.00	0.00	0.00	69 000.00	0.00	602 619.00	0.00	0.00	636 322.25	3 181 611.25	50	1 590 805.63	1 590 805.63	1 590 805.63
14 - C-PATH	695 500.00	0.00	0.00	0.00	15 360.00	0.00	28 821.00	0.00	0.00	184 920.25	924 601.25	50	462 300.63	462 300.63	462 300.63
15 - VHIR	860 821.00	0.00	0.00	0.00	9 000.00	0.00	364 619.00	0.00	0.00	308 610.00	1 543 050.00	50	771 525.00	771 525.00	771 525.00
16 - LUMC	862 164.00	0.00	0.00	0.00	137 160.00	0.00	38 400.00	0.00	0.00	259 431.00	1 297 155.00	50	648 577.50	648 577.50	648 577.50
17 - UTWENTE	296 836.00	0.00	0.00	0.00	4 860.00	0.00	0.00	0.00	0.00	75 424.00	377 120.00	50	188 560.00	188 560.00	188 560.00
18 - UPM	846 643.00	0.00	0.00	0.00	10 860.00	0.00	4 000.00	0.00	0.00	215 375.75	1 076 878.75	50	538 439.38	538 439.38	538 439.38
19 - UMCG	1 265 993.00	0.00	0.00	0.00	4 860.00	0.00	4 000.00	0.00	0.00	318 713.25	1 593 566.25	50	796 783.13	796 783.13	796 783.13
20 - AUMC	525 179.00	0.00	0.00	0.00	5 860.00	0.00	4 000.00	0.00	0.00	133 759.75	668 798.75	50	334 399.38	334 399.38	334 399.38
21 - UM	288 000.00	0.00	0.00	0.00	5 860.00	0.00	0.00	0.00	0.00	73 465.00	367 325.00	50	183 662.50	183 662.50	183 662.50
22 - EATRIS	564 975.00	0.00	0.00	25 000.00	60 053.00	0.00	168 340.00	0.00	0.00	198 342.00	1 016 710.00	50	508 355.00	508 355.00	508 355.00
23 - FGB	600 375.00	0.00	0.00	0.00	34 253.00	0.00	4 000.00	0.00	0.00	159 657.00	798 285.00	50	399 142.50	399 142.50	399 142.50
24 - APHP	1 034 133.00	0.00	0.00	0.00	48 750.00	0.00	210 583.00	0.00	0.00	323 366.50	1 616 832.50	50	808 416.25	808 416.25	808 416.25
25 - UHASSELT	230 100.00	0.00	0.00	0.00	3 000.00	0.00	2 250.00	0.00	0.00	58 837.50	294 187.50	50	147 093.75	147 093.75	147 093.75
26 - EURORDIS	877 753.00	0.00	0.00	0.00	272 100.00	0.00	147 800.00	0.00	0.00	324 413.25	1 622 066.25	50	811 033.13	811 033.13	811 033.13
27 - VULSK	506 060.00	0.00	0.00	0.00	56 680.00	0.00	23 040.00	0.00	0.00	146 445.00	732 225.00	50	366 112.50	366 112.50	366 112.50
28 - UC	372 138.00	0.00	0.00	0.00	3 000.00	0.00	231 286.00	0.00	0.00	151 606.00	758 030.00	50	379 015.00	379 015.00	379 015.00
29 - FFRD	931 371.00	0.00	0.00	0.00	32 660.00	0.00	369 390.00	300 000.00	0.00	333 355.25	1 966 776.25	50	983 388.13	983 388.13	983 388.13

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	Estimated eligible[1] costs (per budget category)											Estimated EU contribution[2]			
	Direct costs									Indirect costs	Total costs	EU contribution to eligible costs			Maximum grant amount[6]
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories		E. Indirect costs[3]		Funding rate %[4]	Maximum EU contribution[5]	Requested EU contribution	
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	D.1 Financial support to third parties	D.2 Internally invoiced goods and services	E. Indirect costs					
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[7]	Actual costs	Actual costs	Actual costs	Actual costs	Actual costs	Unit costs (usual accounting practices)	Flat-rate costs[8]					
	a1	a2	a3	b	c1	c2	c3	d1	d2	e = 0,25 * (a1 + a2 + a3 + c1 + c2 + c3)	f = a+b+c+d+e	U	g = f * U%	h	m
30 - AFM	288 600.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	72 900.00	364 500.00	50	182 250.00	182 250.00	182 250.00
31 - CCUH	126 000.00	0.00	0.00	0.00	27 420.00	0.00	35 064.00	0.00	0.00	47 121.00	235 605.00	50	117 802.50	117 802.50	117 802.50
32 - AICIB	123 336.00	0.00	0.00	0.00	5 000.00	0.00	0.00	0.00	0.00	32 084.00	160 420.00	50	80 210.00	80 210.00	80 210.00
33 - IMGGE	40 158.00	0.00	0.00	0.00	5 000.00	0.00	0.00	0.00	0.00	11 289.50	56 447.50	50	28 223.75	28 223.75	28 223.75
34 - RDI	124 900.00	0.00	0.00	0.00	3 000.00	0.00	50 000.00	0.00	0.00	44 475.00	222 375.00	50	111 187.50	111 187.50	111 187.50
35 - ACU	11 357.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	3 589.25	17 946.25	50	8 973.13	8 973.13	8 973.13
36 - AIT	221 143.00	0.00	0.00	0.00	4 860.00	0.00	0.00	0.00	0.00	56 500.75	282 503.75	50	141 251.88	141 251.88	141 251.88
37 - AMU	171 600.00	0.00	0.00	0.00	5 560.00	0.00	0.00	0.00	0.00	44 290.00	221 450.00	50	110 725.00	110 725.00	110 725.00
38 - AOU Meyer IRCCS	58 500.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	15 375.00	76 875.00	50	38 437.50	38 437.50	38 437.50
39 - ASU-FC	227 500.00	0.00	0.00	0.00	17 800.00	0.00	18 880.00	0.00	0.00	66 045.00	330 225.00	50	165 112.50	165 112.50	165 112.50
40 - BIU	18 837.00	0.00	0.00	0.00	3 000.00	0.00	57 857.00	0.00	0.00	19 923.50	99 617.50	50	49 808.75	49 808.75	49 808.75
41 - BMBF	0.00	0.00	0.00	0.00	3 000.00	0.00	4 000.00	9 000 000.00	0.00	1 750.00	9 008 750.00	50	4 504 375.00	2 683 005.99	2 683 005.99
42 - CCRI GmbH	234 000.00	0.00	0.00	0.00	11 880.00	0.00	0.00	0.00	0.00	61 470.00	307 350.00	50	153 675.00	153 675.00	153 675.00
43 - CENTOGENE	117 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	30 000.00	150 000.00	50	75 000.00	75 000.00	75 000.00
44 - CHARITE	399 516.00	0.00	0.00	0.00	3 000.00	0.00	122 485.00	0.00	0.00	131 250.25	656 251.25	50	328 125.63	328 125.63	328 125.63
45 - CHI	126 828.00	0.00	0.00	0.00	3 000.00	0.00	80 571.00	0.00	0.00	52 599.75	262 998.75	50	131 499.38	131 499.38	131 499.38
46 - CHU Dijon	175 500.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	44 625.00	223 125.00	50	111 562.50	111 562.50	111 562.50
47 - CE	398 574.00	0.00	0.00	0.00	3 000.00	0.00	4 000.00	0.00	0.00	101 393.50	506 967.50	50	253 483.75	253 483.75	253 483.75
48 - REGIONH	117 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	30 000.00	150 000.00	50	75 000.00	75 000.00	75 000.00
49 - CSO-MOH	134 420.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	960 000.00	0.00	37 020.00	1 145 100.00	50	572 550.00	434 008.01	434 008.01
50 - CVBF	213 820.00	0.00	0.00	0.00	8 000.00	0.00	0.00	0.00	0.00	55 455.00	277 275.00	50	138 637.50	138 637.50	138 637.50
51 - DDF	220 000.00	0.00	0.00	0.00	7 860.00	0.00	0.00	0.00	0.00	56 965.00	284 825.00	50	142 412.50	142 412.50	142 412.50
52 - ELS	0.00	0.00	0.00	0.00	3 000.00	0.00	333 960.00	0.00	0.00	84 240.00	421 200.00	50	210 600.00	210 600.00	210 600.00
53 - Erasmus MC	440 050.00	0.00	0.00	0.00	6 000.00	0.00	208 333.00	0.00	0.00	163 595.75	817 978.75	50	408 989.38	408 989.38	408 989.38
54 - F.R.S.-FNRS	18 000.00	0.00	0.00	0.00	9 660.00	0.00	0.00	900 000.00	0.00	6 915.00	934 575.00	50	467 287.50	283 821.89	283 821.89
55 - FHG	0.00	472 465.50	0.00	0.00	3 000.00	0.00	136 587.00	0.00	0.00	153 013.13	765 065.63	50	382 532.82	382 532.82	382 532.82
56 - FRRB	12 400.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	4 500 000.00	0.00	6 515.00	4 532 575.00	50	2 266 287.50	1 282 839.44	1 282 839.44
57 - ECRIN	31 500.00	0.00	0.00	0.00	11 600.00	0.00	3 180.00	0.00	0.00	11 570.00	57 850.00	50	28 925.00	28 925.00	28 925.00
58 - FWF	24 400.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	2 700 000.00	0.00	9 515.00	2 747 575.00	50	1 373 787.50	794 930.67	794 930.67
59 - IFD	13 000.00	0.00	0.00	0.00	8 180.00	0.00	4 000.00	3 000 000.00	0.00	6 295.00	3 031 475.00	50	1 515 737.50	864 008.80	864 008.80
60 - FSJD-CERCA	150 228.00	0.00	0.00	0.00	3 000.00	0.00	7 878.00	0.00	0.00	40 276.50	201 382.50	50	100 691.25	100 691.25	100 691.25
61 - FCT	9 500.00	0.00	0.00	0.00	9 660.00	0.00	0.00	1 050 000.00	0.00	4 790.00	1 073 950.00	50	536 975.00	316 043.45	316 043.45
62 - MZd	0.00	0.00	0.00	0.00	0.00	0.00	4 000.00	1 500 000.00	0.00	1 000.00	1 505 000.00	50	752 500.00	439 620.90	439 620.90
62.1 - AZV	4 958.00	0.00	0.00	0.00	8 180.00	0.00	0.00	0.00	0.00	3 284.50	16 422.50	50	8 211.25	8 211.25	8 211.25

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	Estimated eligible[1] costs (per budget category)											Estimated EU contribution[2]			
	Direct costs									Indirect costs	Total costs	EU contribution to eligible costs			Maximum grant amount[6]
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories		E. Indirect costs[3]		Funding rate %[4]	Maximum EU contribution[5]	Requested EU contribution	
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	D.1 Financial support to third parties	D.2 Internally invoiced goods and services	E. Indirect costs					
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[7]	Actual costs	Actual costs	Actual costs	Actual costs	Actual costs	Unit costs (usual accounting practices)	Flat-rate costs[8]					
	a1	a2	a3	b	c1	c2	c3	d1	d2	e = 0,25 * (a1 + a2 + a3 + c1 + c2 + c3)	f = a+b+c+d+e	U	g = f * U%	h	m
63 - GNT	601 128.00	0.00	0.00	0.00	3 000.00	0.00	114 214.00	0.00	0.00	179 585.50	897 927.50	50	448 963.75	448 963.75	448 963.75
64 - GERAD	29 575.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	8 143.75	40 718.75	50	20 359.38	20 359.38	20 359.38
65 - RS	27 300.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	7 575.00	37 875.00	50	18 937.50	18 937.50	18 937.50
66 - GUF	61 521.00	0.00	0.00	0.00	4 860.00	0.00	0.00	0.00	0.00	16 595.25	82 976.25	50	41 488.13	41 488.13	41 488.13
67 - HRB	136 992.00	0.00	0.00	0.00	18 540.00	0.00	4 000.00	1 500 000.00	0.00	39 883.00	1 699 415.00	50	849 707.50	597 314.15	597 314.15
68 - İBG	317 917.00	0.00	0.00	0.00	25 580.00	0.00	12 200.00	0.00	0.00	88 924.25	444 621.25	50	222 310.63	222 310.63	222 310.63
69 - Rannis	18 000.00	0.00	0.00	0.00	9 660.00	0.00	0.00	428 571.00	0.00	6 915.00	463 146.00	50	231 573.00	150 500.42	150 500.42
70 - IMAGINE	313 703.00	0.00	0.00	0.00	15 833.00	0.00	44 974.00	0.00	4 286.00	93 627.50	472 423.50	50	236 211.75	236 211.75	236 211.75
71 - IGC PAN	39 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	10 500.00	52 500.00	50	26 250.00	26 250.00	26 250.00
72 - ISCIII	468 687.00	0.00	0.00	0.00	20 020.00	0.00	11 628.00	4 800 000.00	0.00	125 083.75	5 425 418.75	50	2 712 709.38	1 899 967.27	1 899 967.27
73 - INSA	58 968.00	0.00	0.00	0.00	11 880.00	0.00	0.00	0.00	0.00	17 712.00	88 560.00	50	44 280.00	44 280.00	44 280.00
74 - IOR	19 500.00	0.00	0.00	0.00	3 000.00	0.00	3 500.00	0.00	0.00	6 500.00	32 500.00	50	16 250.00	16 250.00	16 250.00
75 - ISS	65 250.00	0.00	0.00	0.00	39 260.00	0.00	13 940.00	0.00	0.00	29 612.50	148 062.50	50	74 031.25	74 031.25	74 031.25
76 - IT-MOH	13 000.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	3 000 000.00	0.00	6 665.00	3 033 325.00	50	1 516 662.50	865 673.80	865 673.80
77 - KU Leuven	341 055.00	0.00	0.00	0.00	3 000.00	0.00	83 978.00	0.00	0.00	107 008.25	535 041.25	50	267 520.63	267 520.63	267 520.63
78 - LZP	8 000.00	0.00	0.00	0.00	9 660.00	0.00	0.00	300 000.00	0.00	4 415.00	322 075.00	50	161 037.50	103 435.63	103 435.63
79 - MRT	216 000.00	0.00	0.00	0.00	5 360.00	0.00	0.00	0.00	0.00	55 340.00	276 700.00	50	138 350.00	138 350.00	138 350.00
80 - MUS	39 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	10 500.00	52 500.00	50	26 250.00	26 250.00	26 250.00
81 - MUH	234 000.00	0.00	0.00	0.00	16 880.00	0.00	0.00	0.00	0.00	62 720.00	313 600.00	50	156 800.00	156 800.00	156 800.00
82 - MUR	9 000.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	3 000 000.00	0.00	5 665.00	3 028 325.00	50	1 514 162.50	861 173.80	861 173.80
83 - NCBR	7 000.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	3 600 000.00	0.00	5 165.00	3 625 825.00	50	1 812 912.50	1 026 060.06	1 026 060.06
84 - NKUA	39 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	10 500.00	52 500.00	50	26 250.00	26 250.00	26 250.00
85 - MoH SR	78 000.00	0.00	0.00	0.00	11 880.00	0.00	0.00	0.00	0.00	22 470.00	112 350.00	50	56 175.00	56 175.00	56 175.00
86 - RDG	52 000.00	0.00	0.00	0.00	11 880.00	0.00	0.00	0.00	0.00	15 970.00	79 850.00	50	39 925.00	39 925.00	39 925.00
87 - REGIONSYD	117 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	30 000.00	150 000.00	50	75 000.00	75 000.00	75 000.00
88 - OPBG	136 500.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	34 875.00	174 375.00	50	87 187.50	87 187.50	87 187.50
89 - OSR	184 548.00	0.00	0.00	0.00	3 000.00	0.00	315 314.00	0.00	0.00	125 715.50	628 577.50	50	314 288.75	314 288.75	314 288.75
90 - JSI	50 400.00	0.00	0.00	0.00	11 880.00	0.00	0.00	0.00	0.00	15 570.00	77 850.00	50	38 925.00	38 925.00	38 925.00
91 - RCN	17 000.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	1 542 857.00	0.00	7 665.00	1 581 182.00	50	790 591.00	464 271.41	464 271.41
92 - FWO	18 000.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	2 100 000.00	0.00	7 915.00	2 139 575.00	50	1 069 787.50	620 594.41	620 594.41
93 - REUH	117 200.00	0.00	0.00	0.00	33 000.00	0.00	1 660.00	0.00	0.00	37 965.00	189 825.00	50	94 912.50	94 912.50	94 912.50
94 - RIF	17 106.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	3 000 000.00	0.00	7 691.50	3 038 457.50	50	1 519 228.75	870 292.51	870 292.51
95 - RCSI	58 500.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	15 375.00	76 875.00	50	38 437.50	38 437.50	38 437.50
96 - RSU	21 688.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	6 172.00	30 860.00	50	15 430.00	15 430.00	15 430.00

	Estimated eligible[1] costs (per budget category)											Estimated EU contribution[2]			
	Direct costs									Indirect costs	Total costs	EU contribution to eligible costs			Maximum grant amount[6]
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories		E. Indirect costs[3]		Funding rate %[4]	Maximum EU contribution[5]	Requested EU contribution	
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	D.1 Financial support to third parties	D.2 Internally invoiced goods and services	E. Indirect costs					
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[7]	Actual costs	Actual costs	Actual costs	Actual costs	Actual costs	Unit costs (usual accounting practices)	Flat-rate costs[8]					
	a1	a2	a3	b	c1	c2	c3	d1	d2	e = 0,25 * (a1 + a2 + a3 + c1 + c2 + c3)	f = a+b+c+d+e	U	g = f * U%	h	m
97 - Sciensano	312 000.00	0.00	0.00	0.00	13 500.00	0.00	0.00	0.00	0.00	81 375.00	406 875.00	50	203 437.50	203 437.50	203 437.50
98 - SPW	18 000.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	3 000 000.00	0.00	7 915.00	3 039 575.00	50	1 519 787.50	871 298.80	871 298.80
99 - SFU	192 300.00	0.00	0.00	0.00	20 200.00	0.00	8 610.00	0.00	0.00	55 277.50	276 387.50	50	138 193.75	138 193.75	138 193.75
100 - ETAg	7 000.00	0.00	0.00	0.00	9 660.00	0.00	0.00	150 000.00	0.00	4 165.00	170 825.00	50	85 412.50	60 526.56	60 526.56
101 - SAS	7 000.00	0.00	0.00	0.00	9 660.00	0.00	0.00	120 000.00	0.00	4 165.00	140 825.00	50	70 412.50	52 169.75	52 169.75
102 - Sonio	175 500.00	0.00	0.00	0.00	5 360.00	0.00	0.00	0.00	0.00	45 215.00	226 075.00	50	113 037.50	113 037.50	113 037.50
103 - MOSAE	7 400.00	0.00	0.00	0.00	9 660.00	0.00	0.00	150 000.00	0.00	4 265.00	171 325.00	50	85 662.50	60 976.56	60 976.56
104 - SRC	14 212.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	1 457 143.00	0.00	6 968.00	1 491 983.00	50	745 991.50	437 258.38	437 258.38
105 - TEDDY	39 000.00	0.00	0.00	0.00	18 440.00	0.00	0.00	0.00	0.00	14 360.00	71 800.00	50	35 900.00	35 900.00	35 900.00
106 - TEKKARE	429 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	108 000.00	540 000.00	50	270 000.00	270 000.00	270 000.00
107 - TIF	48 000.00	0.00	0.00	0.00	11 880.00	0.00	0.00	0.00	0.00	14 970.00	74 850.00	50	37 425.00	37 425.00	37 425.00
108 - TUBITAK	22 560.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	1 500 000.00	0.00	9 055.00	1 545 275.00	50	772 637.50	458 588.15	458 588.15
109 - RT (TuscReg)	16 114.00	0.00	0.00	0.00	9 660.00	0.00	0.00	900 000.00	0.00	6 443.50	932 217.50	50	466 108.75	281 700.20	281 700.20
110 - UAB	129 558.00	0.00	0.00	0.00	3 000.00	0.00	19 286.00	0.00	0.00	37 961.00	189 805.00	50	94 902.50	94 902.50	94 902.50
111 - UCD	43 504.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	11 626.00	58 130.00	50	29 065.00	29 065.00	29 065.00
112 - UCSC	103 071.00	0.00	0.00	0.00	14 700.00	0.00	12 200.00	0.00	0.00	32 492.75	162 463.75	50	81 231.88	81 231.88	81 231.88
113 - UEF	174 408.00	0.00	0.00	0.00	3 000.00	0.00	52 800.00	0.00	0.00	57 552.00	287 760.00	50	143 880.00	143 880.00	143 880.00
114 - UKA	97 200.00	0.00	0.00	0.00	3 000.00	0.00	2 250.00	0.00	0.00	25 612.50	128 062.50	50	64 031.25	64 031.25	64 031.25
115 - UKLFR	246 168.00	0.00	0.00	0.00	6 000.00	0.00	68 571.00	0.00	0.00	80 184.75	400 923.75	50	200 461.88	200 461.88	200 461.88
116 - UNICAMPANIA	58 500.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	15 375.00	76 875.00	50	38 437.50	38 437.50	38 437.50
117 - UoC	39 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	10 500.00	52 500.00	50	26 250.00	26 250.00	26 250.00
118 - UGENT	156 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	39 750.00	198 750.00	50	99 375.00	99 375.00	99 375.00
119 - UKCL	58 500.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	15 375.00	76 875.00	50	38 437.50	38 437.50	38 437.50
120 - WDO	149 243.00	0.00	0.00	0.00	5 220.00	0.00	0.00	0.00	0.00	38 615.75	193 078.75	50	96 539.38	96 539.38	96 539.38
121 - UU	388 000.00	0.00	0.00	0.00	4 860.00	0.00	2 250.00	0.00	0.00	98 777.50	493 887.50	50	246 943.75	246 943.75	246 943.75
122 - c4c-S	66 857.00	0.00	0.00	0.00	14 180.00	0.00	4 260.00	0.00	0.00	21 324.25	106 621.25	50	53 310.63	53 310.63	53 310.63
123 - CAU	52 195.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	13 798.75	68 993.75	50	34 496.88	34 496.88	34 496.88
124 - CNRS	129 168.00	0.00	0.00	0.00	3 000.00	0.00	37 714.00	0.00	0.00	42 470.50	212 352.50	50	106 176.25	106 176.25	106 176.25
125 - CIBER	175 188.00	0.00	0.00	0.00	3 000.00	0.00	81 969.00	0.00	0.00	65 039.25	325 196.25	50	162 598.13	162 598.13	162 598.13
126 - UEFISCDI	11 760.00	0.00	0.00	0.00	9 660.00	0.00	4 000.00	3 000 000.00	0.00	6 355.00	3 031 775.00	50	1 515 887.50	864 278.80	864 278.80
127 - UNIROMA1	65 143.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	17 035.75	85 178.75	50	42 589.38	42 589.38	42 589.38
128 - UANTWERPEN	39 000.00	0.00	0.00	0.00	2 000.00	0.00	0.00	0.00	0.00	10 250.00	51 250.00	50	25 625.00	25 625.00	25 625.00
129 - BNSF	13 000.00	0.00	0.00	0.00	9 660.00	0.00	0.00	225 000.00	0.00	5 665.00	253 325.00	50	126 662.50	88 168.60	88 168.60
130 - Aalborg UH	39 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	10 500.00	52 500.00	50	26 250.00	26 250.00	26 250.00

	Estimated eligible[1] costs (per budget category)											Estimated EU contribution[2]			
	Direct costs									Indirect costs	Total costs	EU contribution to eligible costs			Maximum grant amount[6]
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories		E. Indirect costs[3]		Funding rate %[4]	Maximum EU contribution[5]	Requested EU contribution	
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	D.1 Financial support to third parties	D.2 Internally invoiced goods and services	E. Indirect costs					
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[7]	Actual costs	Actual costs	Actual costs	Actual costs	Actual costs	Unit costs (usual accounting practices)	Flat-rate costs[8]					
	a1	a2	a3	b	c1	c2	c3	d1	d2	e = 0,25 * (a1 + a2 + a3 + c1 + c2 + c3)	f = a+b+c+d+e	U	g = f * U%	h	m
131 - RDB	22 860.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	6 465.00	32 325.00	50	16 162.50	16 162.50	16 162.50
132 - BBMRI-ERIC	84 643.00	0.00	0.00	0.00	4 860.00	0.00	0.00	0.00	0.00	22 375.75	111 878.75	50	55 939.38	55 939.38	55 939.38
133 - AarhusUH	58 500.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	15 375.00	76 875.00	50	38 437.50	38 437.50	38 437.50
134 - IABS-EU	76 050.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	19 762.50	98 812.50	50	49 406.25	49 406.25	49 406.25
135 - HRCI	35 100.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	9 525.00	47 625.00	50	23 812.50	23 812.50	23 812.50
136 - LMU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	50	0.00	0.00	0.00
136.1 - KUM	266 500.00	0.00	0.00	0.00	30 500.00	0.00	208 333.00	0.00	0.00	126 333.25	631 666.25	50	315 833.13	315 833.13	315 833.13
137 - MSW	249 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	63 000.00	315 000.00	50	157 500.00	157 500.00	157 500.00
138 - FNR	21 792.00	0.00	0.00	0.00	9 660.00	0.00	0.00	990 000.00	0.00	7 863.00	1 029 315.00	50	514 657.50	313 158.33	313 158.33
139 - NKFIH	8 000.00	0.00	0.00	0.00	9 660.00	0.00	0.00	900 000.00	0.00	4 415.00	922 075.00	50	461 037.50	272 571.89	272 571.89
140 - PEI	164 950.50	0.00	0.00	0.00	3 000.00	0.00	37 705.00	0.00	0.00	51 413.88	257 069.38	50	128 534.69	128 534.69	128 534.69
141 - PLUS	196 728.00	0.00	0.00	0.00	5 250.00	0.00	52 000.00	0.00	0.00	63 494.50	317 472.50	50	158 736.25	158 736.25	158 736.25
142 - SU	16 250.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	4 812.50	24 062.50	50	12 031.25	12 031.25	12 031.25
143 - UNISI	58 500.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	15 375.00	76 875.00	50	38 437.50	38 437.50	38 437.50
144 - Vinnova	17 000.00	0.00	0.00	0.00	9 660.00	0.00	0.00	1 414 286.00	0.00	6 665.00	1 447 611.00	50	723 805.50	425 956.62	425 956.62
145 - CRG-CERCA	110 400.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	28 350.00	141 750.00	50	70 875.00	70 875.00	70 875.00
146 - GMS-RS	27 300.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	7 575.00	37 875.00	50	18 937.50	18 937.50	18 937.50
147 - VIB	19 500.00	0.00	0.00	0.00	1 000.00	0.00	0.00	0.00	0.00	5 125.00	25 625.00	50	12 812.50	12 812.50	12 812.50
148 - IPG	39 000.00	0.00	0.00	0.00	3 000.00	0.00	0.00	0.00	0.00	10 500.00	52 500.00	50	26 250.00	26 250.00	26 250.00
149 - UO	39 000.00	0.00	0.00	0.00	11 880.00	0.00	0.00	0.00	0.00	12 720.00	63 600.00	50	31 800.00	31 800.00	31 800.00
150 - HSJD	45 500.00	0.00	0.00	0.00	3 000.00	0.00	3 500.00	0.00	0.00	13 000.00	65 000.00	50	32 500.00	32 500.00	32 500.00
151 - AZ															
152 - CHEO-RI															
153 - CIHR															
154 - DFG															
155 - FDB															
156 - FRQS															
157 - HIPRA															
158 - LAB HIPRA															
159 - MICYRN															
160 - Miltenyi															
161 - Pfizer															
162 - RCC															
163 - REI															

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	Estimated eligible[1] costs (per budget category)											Estimated EU contribution[2]			
	Direct costs									Indirect costs	Total costs	EU contribution to eligible costs			Maximum grant amount[6]
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories		E. Indirect costs[3]		Funding rate %[4]	Maximum EU contribution[5]	Requested EU contribution	
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	D.1 Financial support to third parties	D.2 Internally invoiced goods and services	E. Indirect costs					
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[7]	Actual costs	Actual costs	Actual costs	Actual costs	Actual costs	Unit costs (usual accounting practices)	Flat-rate costs[8]					
	a1	a2	a3	b	c1	c2	c3	d1	d2	e = 0,25 * (a1 + a2 + a3 + c1 + c2 + c3)	f = a+b+c+d+e	U	g = f * U%	h	m
164 - RJF															
165 - ROCHE															
166 - SNSF															
167 - UCB															
168 - Fraunhofer UK															
169 - GA UK															
170 - UNEW															
171 - CUH															
172 - ULEIC															
173 - QUB-UK															
174 - UCL															
175 - UCAM															
Total consortium	40 373 906.07	472 465.50	0.00	142 857.00	2 175 119.00	9 000.00	7 369 205.00	82 673 571.00	14 572.00	12 599 923.90	145 830 619.47		72 915 309.90	56 317 412.61	56 317 412.61

[1] See Article 6 for the eligibility conditions. All amounts must be expressed in EUR (see Article 21 for the conversion rules).
[2] The consortium remains free to decide on a different internal distribution of the EU funding (via the consortium agreement; see Article 7).
[3] Indirect costs already covered by an operating grant (received under any EU funding programme) are ineligible (see Article 6.3). Therefore, a beneficiary/affiliated entity that receives an operating grant during the action duration cannot declare indirect costs for the year(s)/reporting period(s) covered by the operating grant, unless they can demonstrate that the operating grant does not cover any costs of the action. This requires specific accounting tools. Please immediately contact us via the EU Funding & Tenders Portal for details.
[4] See Data Sheet for the funding rate(s).
[5] This is the theoretical amount of the EU contribution to costs, if the reimbursement rate is applied to all the budgeted costs. This theoretical amount is then capped by the 'maximum grant amount'.
[6] The 'maximum grant amount' is the maximum grant amount decided by the EU. It normally corresponds to the requested grant, but may be lower.
[7] See Annex 2a 'Additional information on the estimated budget' for the details (units, cost per unit).
[8] See Data Sheet for the flat-rate.

ANNEX 2a

ADDITIONAL INFORMATION ON UNIT COSTS AND CONTRIBUTIONS

SME owners/natural person beneficiaries without salary (Decision C(2020) 7115[1])

Type: unit costs

Units: days spent working on the action (rounded up or down to the nearest half-day)

Amount per unit (daily rate): calculated according to the following formula:

{EUR 5 080 / 18 days = **282,22**}
multiplied by
{country-specific correction coefficient of the country where the beneficiary is established}

The country-specific correction coefficients used are those set out in the Horizon Europe Work Programme (section Marie Skłodowska-Curie actions) in force at the time of the call (see Portal Reference Documents).

HE and Euratom Research Infrastructure actions[2]

Type: unit costs

Units[3]: see (for each access provider and installation) the unit cost table in Annex 2b

Amount per unit*: see (for each access provider and installation) the unit cost table in Annex 2b

* Amount calculated as follows:

For trans-national access:

$$\frac{\text{average annual total trans-national access costs to the installation (over past two years[4])}}{\text{average annual total quantity of trans-national access to the installation (over past two years[5])}}$$

For virtual access:

$$\frac{\text{total virtual access costs to the installation (over the last year[6])}}{\text{total quantity of virtual access to the installation (over the last year[7])}}$$

Euratom staff mobility costs[8]

Monthly living allowance

Type: unit costs

---

1 Commission Decision of 20 October 2020 authorising the use of unit costs for the personnel costs of the owners of small and medium-sized enterprises and beneficiaries that are natural persons not receiving a salary for the work carried out by themselves under an action or work programme (C(2020)7715).

2 Decision of 19 April 2021 authorising the use of unit costs for the costs of providing trans-national and virtual access in Research Infrastructure actions under the Horizon Europe Programme (2021-2027) and the Research and Training Programme of the European Atomic Energy Community (2021-2025).

3 Unit of access (e.g. beam hours, weeks of access, sample analysis) fixed by the access provider in proposal.

4 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

5 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

6 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

7 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

8 Decision of 15 March 2021 authorising the use of unit costs for mobility in co-fund actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025).

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit*: see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

* Amount calculated as follows from 1 January 2021:
{**EUR 4 300** multiplied by
country-specific correction coefficient** of the country where the staff member is seconded}[9]

**Country-specific correction coefficients as from 1 January 2021[10]

EU-Member States[11]

Country / Place	Coefficient (%)
Bulgaria	59,1
Czech Rep.	85,2
Denmark	131,3
Germany Bonn Karlsruhe Munich	101,9 95,8 98 113,9
Estonia	82,3
Ireland	129
Greece	81,4
Spain	94,2
France	120,5
Croatia	75,8
Italy Varese	95 90,7
Cyprus	78,2
Latvia	77,5
Lithuania	76,6
Hungary	71,9
Malta	94,7
Netherlands	113,9
Austria	107,9
Poland	70,9
Portugal	91,1
Romania	66,6
Slovenia	86,1

[9] Unit costs for living allowances are calculated by using a method of calculation similar to that applied for the secondment to the European Commission of seconded national experts (SNEs).

[10] For the financial statements, the amount must be adjusted according to the actual place of secondment.
The revised coefficients were adopted in the Decision authorising the use of unit costs for the Fusion Programme co-fund action under the Research and training Programme of the European Atomic Energy Community 2021-2025. They are based on the 2020 Annual update of the remuneration and pensions of the officials and other servants of the European Union and the correction coefficients applied thereto (OJ C 428, 11.12.2020) to ensure purchasing power parity. The revised coefficient are applied as from 1 January 2021 through an amendment to the grant agreement.

[11] No correction coefficient shall be applicable in Belgium and Luxembourg.

Slovakia	80,6
Finland	118,4
Sweden	124,3

Third countries

Country/place	Coefficient (%)
China	82,2
India	72,3
Japan	111,8
Russia	92,7
South Korea	92,3
Switzerland	129.2
Ukraine	82.3
United Kingdom	97.6
United States	101,4 (New-York) 90,5 (Washington)

Mobility allowance

Type: Unit costs

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit: **EUR 600** per person-month; see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

Family allowance

Type: unit costs

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit: **EUR 660** per person-month; see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

Education allowance

Type: Unit costs

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit*: see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

*Amount calculated as follows from 1 January 2021:
{EUR 283.82 x number of dependent children[12]**}**

[12] For the estimated budget (Annex 2): an average should be used. (⚠ For the financial statements, the number of children (and months) must be adjusted according to the actual family status at the moment the secondment starts.)

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

TEAMIT RESEARCH SL (TEAMIT), PIC 896104237, established in PASSE DE GRACIA 58 PLANTA 4 PUERTA 2, BARCELONA 08007, Spain,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

DEUTSCHES ZENTRUM FUR LUFT - UND RAUMFAHRT EV (DLR), PIC 999981731, established in LINDER HOHE, KOLN 51147, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

AGENCE NATIONALE DE LA RECHERCHE (ANR), PIC 998711613, established in 86 RUE REGNAULT, PARIS 75013, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FONDAZIONE TELETHON ETS (FTELE), PIC 999448716, established in VIA VARESE 16/B, ROMA 00185, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

Lietuvos mokslo taryba (LMT), PIC 997808446, established in Gedimino 3, Vilnius LT-01103, Lithuania,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ZORGONDERZOEK NEDERLAND ZON (ZonMw), PIC 999544164, established in Laan Van Nieuw Oost Indie 334, DEN HAAG 2593 CE, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

EBERHARD KARLS UNIVERSITAET TUEBINGEN (UT), PIC 999991916, established in GESCHWISTER-SCHOLL-PLATZ, TUEBINGEN 72074, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

TARTU ULIKOOL (UTARTU), PIC 999895013, established in ULIKOOLI 18, TARTU 50090, Estonia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CONSORCIO PARA LA EXPLOTACION DEL CENTRO NACIONAL DE ANALISIS GENOMICO (CNAG), PIC 882802433, established in C BALDIRI 1 REIXAC 4, BARCELONA 08028, Spain,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

STICHTING RADBOUD UNIVERSITAIR MEDISCH CENTRUM (SRUMC), PIC 892057785, established in GEERT GROOTEPLEIN 10 ZUID, NIJMEGEN 6525 GA, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

TECHNISCHE UNIVERSITAET MUENCHEN (TUM), PIC 999977463, established in Arcisstrasse 21, MUENCHEN 80333, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITATSKLINIKUM HEIDELBERG (UKHD), PIC 999841081, established in IM NEUENHEIMER FELD 672, HEIDELBERG 69120, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CRITICAL PATH INSTITUTE STICHTING (C-PATH), PIC 887895418, established in BARBARA STROZZILAAN 101, AMSTERDAM 1083 HN, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FUNDACIO HOSPITAL UNIVERSITARI VALL D'HEBRON - INSTITUT DE RECERCA (VHIR), PIC 999541642, established in PASSEIG VALL D HEBRON 119-129 EDIFICIO DE RECERCA, BARCELONA 08035, Spain,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ACADEMISCH ZIEKENHUIS LEIDEN (LUMC), PIC 999990849, established in ALBINUSDREEF 2, LEIDEN 2333 ZA, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITEIT TWENTE (UTWENTE), PIC 999900833, established in DRIENERLOLAAN 5, ENSCHEDE 7522 NB, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSIDAD POLITECNICA DE MADRID (UPM), PIC 999974844, established in CALLE RAMIRO DE MAEZTU 7 EDIFICIO RECTORADO, MADRID 28040, Spain,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ACADEMISCH ZIEKENHUIS GRONINGEN (UMCG), PIC 999914801, established in HANZEPLEIN 1, GRONINGEN 9713 GZ, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

STICHTING AMSTERDAM UMC (AUMC), PIC 919322739, established in DE BOELELAAN 1117, AMSTERDAM 1081 HV, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITEIT MAASTRICHT (UM), PIC 999975911, established in MINDERBROEDERSBERG 4, MAASTRICHT 6200 MD, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

EATRIS ERIC (EATRIS), PIC 941506445, established in DE BOELELAAN 1118, AMSTERDAM 1081 HZ, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FONDAZIONE PER LA RICERCA FARMACOLOGICA GIANNI BENZI ONLUS (FGB), PIC 962478330, established in VIA ABATE EUSTASIO 30, VALENZANO BARI 70010, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ASSISTANCE PUBLIQUE HOPITAUX DE PARIS (APHP), PIC 999645432, established in 55 BOULEVARD DIDEROT, PARIS 75012, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITEIT HASSELT (UHASSELT), PIC 999874934, established in MARTELARENLAAN 42, HASSELT 3500, Belgium,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

EURORDIS - RARE DISEASES EUROPE (EURORDIS), PIC 965288323, established in RUE DIDOT 96, Paris 75014, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

VIESOJI ISTAIGA VILNIAUS UNIVERSITETO LIGONINE SANTAROS KLINIKOS (VULSK), PIC 991636530, established in SANTARISKIU G 2, VILNIUS LT-08661, Lithuania,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSIDADE DE COIMBRA (UC), PIC 997826391, established in PACO DAS ESCOLAS, COIMBRA 3004-531, Portugal,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FONDATION MALADIES RARES (FFRD), PIC 954438485, established in RUE DIDOT 96, PARIS 75014, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ASS FRANCAISE CONTRE LES MYOPATHIES (AFM), PIC 959828387, established in 47-83 47 BOULEVARD DE L'HOPITAL, INSTITUT DE MYOLO, PARIS 75013, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

BERNU KLINISKA UNIVERSITATES SLIMNICA VALSTS SIA (CCUH), PIC 904374748, established in VIENIBAS GATVE 45, RIGA 1004, Latvia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

AICIB - AGENCIA DE INVESTIGACAO CLINICA E INOVACAO BIOMEDICA (AICIB), PIC 892687606, established in RUA DE SANTA CATARINA 1288, PORTO 4000-447, Portugal,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTITUT ZA MOLEKULARNU GENETIKU I GENETICKO INZENJERSTVO (IMGGE), PIC 986427921, established in VOJVODE STEPE 444A, BEOGRAD 11010, Serbia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

RARE DISEASES INTERNATIONAL (RDI), PIC 881348694, established in 96 RUE DIDOT, PARIS 75014, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ACIBADEM MEHMET ALI AYDINLAR UNIVERSITY (ACU), PIC 959704421, established in ICERENKOY MAH. KAYISDAGI CAD. NO/32 ATASEHIR, ISTANBUL 34752, Türkiye,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY GMBH (AIT), PIC 999584128, established in GIEFINGGASSE 4, WIEN 1210, Austria,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITE D'AIX MARSEILLE (AMU), PIC 955518483, established in BOULEVARD CHARLES LIVON 58 LE PHARO, MARSEILLE 13284, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

AZIENDA OSPEDALIERA UNIVERSITARIA MEYER IRCCS (AOU Meyer IRCCS), PIC 998778543, established in VIALE PIERACCINI 24, FIRENZE 50139, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

AZIENDA SANITARIA UNIVERSITARIA FRIULI CENTRALE (ASU-FC), PIC 894464355, established in VIA POZZUOLO 330, UDINE 33100, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

BAR ILAN UNIVERSITY (BIU), PIC 999886574, established in BAR ILAN UNIVERSITY CAMPUS, RAMAT GAN 52900, Israel,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

BUNDESMINISTERIUM FUER BILDUNG UND FORSCHUNG (BMBF), PIC 999835455, established in Heinemannstrasse 2, BONN 53175, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ST. ANNA KINDERKREBSFORSCHUNG GMBH (CCRI GmbH), PIC 891384896, established in ZIMMERMANNPLATZ 10, WIEN 1090, Austria,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CENTOGENE GMBH (CENTOGENE), PIC 878333449, established in AM.STRANDE 7, ROSTOCK 18055, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CHARITE - UNIVERSITAETSMEDIZIN BERLIN (CHARITE), PIC 999992692, established in Chariteplatz 1, BERLIN 10117, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CHECKIMMUNE GMBH (CHI), PIC 889852781, established in CAMPUS VIRCHOW KLINIKUM, CRANACH HAUS AUGUSTENBURG PLATZ 1, BERLIN 13353, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CENTRE HOSPITALIER REG UNIVERSITAIRE DIJON (CHU Dijon), PIC 959994451, established in BOULEVARD MAL DE LATTRE DE TASSIGNY 2, DIJON 21000, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

COPENHAGEN ECONOMICS AS (CE), PIC 938801309, established in LANGEBROGADE 1B, KOBENHAVN K 1411, Denmark,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

REGION HOVEDSTADEN (REGIONH), PIC 999654744, established in KONGENS VAENGE 2, HILLEROD 3400, Denmark,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

MINISTRY OF HEALTH (CSO-MOH), PIC 999596156, established in YIRMIYAHU 39, JERUSALEM 9101002, Israel,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CONSORZIO PER VALUTAZIONI BIOLOGICHE E FARMACOLOGICHE (CVBF), PIC 999717018, established in VIA NICOLO PUTIGNANI 178, BARI 70122, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

STICHTING DUCHENNE DATA FOUNDATION (DDF), PIC 899914882, established in WARMOESDREEF 10, BERGEN OP ZOOM 4614 HC, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ELSEVIER BV (ELS), PIC 999937014, established in RADARWEG 29, AMSTERDAM 1043NX, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ERASMUS UNIVERSITAIR MEDISCH CENTRUM ROTTERDAM (Erasmus MC), PIC 999988424, established in DR MOLEWATERPLEIN 40, ROTTERDAM 3015 GD, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FONDS DE LA RECHERCHE SCIENTIFIQUE- FNRS (F.R.S.-FNRS), PIC 999540381, established in RUE D'EGMONT 5, BRUXELLES 1000, Belgium,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FRAUNHOFER GESELLSCHAFT ZUR FORDERUNG DER ANGEWANDTEN FORSCHUNG EV (FHG), PIC 999984059, established in HANSASTRASSE 27C, MUNCHEN 80686, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FONDAZIONE REGIONALE PER LA RICERCA BIOMEDICA (FRRB), PIC 929009450, established in PIAZZA CITTA DI LOMBARDIA 1, MILANO 20124, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ECRIN EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK (ECRIN), PIC 948646712, established in 30 BD SAINT-JACQUES BATIMENT B, PARIS 75014, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FONDS ZUR FÖRDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG (FWF), PIC 998735960, established in GEORG-COCH-PLATZ 2, WIEN 1010, Austria,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INNOVATIONSFONDEN (IFD), PIC 939076692, established in OSTERGADE 26 A, KOBENHAVN K 1100, Denmark,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FUNDACIO PRIVADA PER A LA RECERCA I LA DOCENCIA SANT JOAN DE DEU (FSJD-CERCA), PIC 999565601, established in SANTA ROSA 39-4, ESPLUGUES DE LLOBREGAT 08950, Spain,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FUNDACAO PARA A CIENCIA E A TECNOLOGIA (FCT), PIC 999543970, established in AVENIDA D CARLOS I 126, LISBOA 1249 074, Portugal,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

MINISTERSTVO ZDRAVOTNICTVI CESKE REPUBLIKY (MZd), PIC 924144512, established in PALACKEHO NAMESTI 375/4, PRAHA 12801, Czechia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ASSOCIATION GENETHON (GNT), PIC 998217883, established in RUE DE L INTERNATIONALE 1 BIS, EVRY 91002, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

GEORGIAN FOUNDATION FOR GENETIC AND RARE DISEASES (GERAD), PIC 953089312, established in TARKHNISHVILI STREET 9 APT 5, TBIILISI 0179, Georgia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

REGION STOCKHOLM (RS), PIC 999522921, established in HANTVERKARGATAN 45, STOCKHOLM 104 22, Sweden,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

JOHANN WOLFGANG GOETHE-UNIVERSITAET FRANKFURT AM MAIN (GUF), PIC 999978724, established in THEODOR W ADORNO PLATZ 1, FRANKFURT AM MAIN 60629, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

THE HEALTH RESEARCH BOARD (HRB), PIC 999546686, established in 67 72 LOWER MOUNT STREET, DUBLIN D02 H638, Ireland,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

IZMIR BIYOTIP VE GENOM MERKEZI (İBG), PIC 906758620, established in MITHATPASA CAD. NO:58/5 BALCOVA, IZMIR 35340, Türkiye,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

RANNSOKNAMIDSTOD ISLANDS (Rannis), PIC 999547268, established in BORGARTUNI 30, REYKJAVIK 105, Iceland,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

IMAGINE INSTITUT DES MALADIES GENETIQUES NECKER ENFANTS MALADES FONDATION (IMAGINE), PIC 955276177, established in 24 BD DU MONTPARNASSE, PARIS 15 75015, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTYTUT GENETYKI CZLOWIEKA POLSKIEJ AKADEMII NAUK (IGC PAN), PIC 982958425, established in STRZESZYNSKA 32, POZNAN 60-479, Poland,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTITUTO DE SALUD CARLOS III (ISCIII), PIC 999507886, established in MONFORTE DE LEMOS 5, MADRID 28029, Spain,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTITUTO NACIONAL DE SAUDE DR. RICARDO JORGE (INSA), PIC 998308190, established in AVENIDA PADRE CRUZ, LISBOA 1649-016, Portugal,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ISTITUTO ORTOPEDICO RIZZOLI (IOR), PIC 999445709, established in VIA DI BARBIANO 1/10, BOLOGNA 40136, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ISTITUTO SUPERIORE DI SANITA (ISS), PIC 999978821, established in Viale Regina Elena 299, ROMA 00161, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

MINISTERO DELLA SALUTE (IT-MOH), PIC 999531942, established in Via Giorgio Ribotta 5, ROMA 00144, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

KATHOLIEKE UNIVERSITEIT LEUVEN (KU Leuven), PIC 999991334, established in OUDE MARKT 13, LEUVEN 3000, Belgium,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

LATVIJAS ZINATNES PADOME (LZP), PIC 999546589, established in SMILSU IELA 8, RIGA LV-1050, Latvia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

MAPI RESEARCH TRUST (MRT), PIC 925695542, established in 27 RUE DE LA VILLETTE, LYON 69003, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

MEDICAL UNIVERSITY SOFIA (MUS), PIC 999857571, established in ACAD IV EVSTATIEV GESHOV ST 15, SOFIA 1431, Bulgaria,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FAKULTNI NEMOCNICE V MOTOLE (MUH), PIC 964458391, established in V UVALU 84, PRAHA 5 150 06, Czechia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

Ministero dell'università e della ricerca (MUR), PIC 894763406, established in Via Michele Carcani 61, Roma 00153, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

NARODOWE CENTRUM BADAN I ROZWOJU (NCBR), PIC 999519720, established in UL. CHMIELNA 69, WARSZAWA 00-801, Poland,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ETHNIKO KAI KAPODISTRIAKO PANEPISTIMIO ATHINON (NKUA), PIC 999643007, established in 6 CHRISTOU LADA STR, ATHINA 10561, Greece,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

MINISTERSTVO ZDRAVOTNICTVA SLOVENSKEJ REPUBLIKY (MoH SR), PIC 999825173, established in LIMBOVA 2, BRATISLAVA 83752, Slovakia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ENOSI SPANION ASTHENON ELLADOS (RDG), PIC 883276763, established in KAPNIKAREAS 19A, ATHINA 105 56, Greece,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

REGION SYDDANMARK (REGIONSYD), PIC 999602073, established in DAMHAVEN 12, VEJLE 7100, Denmark,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

OSPEDALE PEDIATRICO BAMBINO GESU (OPBG), PIC 998837810, established in PIAZZA SANT ONOFRIO 4, ROMA 00165, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

OSPEDALE SAN RAFFAELE SRL (OSR), PIC 953176030, established in VIA OLGETTINA 60, MILANO 20132, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTITUT JOZEF STEFAN (JSI), PIC 999971837, established in Jamova 39, LJUBLJANA 1000, Slovenia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

NORGES FORSKNINGSRAD (RCN), PIC 999460453, established in DRAMMENSVEIEN 288, OSLO 0283, Norway,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FONDS VOOR WETENSCHAPPELIJK ONDERZOEK-VLAANDEREN (FWO), PIC 997949484, established in LEUVENSEWEG 38, BRUSSEL 1000, Belgium,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

RIGAS AUSTRUMU KLINISKA UNIVERSITATES SLIMNICA SIA (REUH), PIC 973366483, established in HIPOKRATA IELA 2, RIGA LV-1079, Latvia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

IDRYMA EREVNAS KAI KAINOTOMIAS (RIF), PIC 999946035, established in ANDREA MICHALAKOPOULOU 29 A, NICOSIA 1075, Cyprus,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ROYAL COLLEGE OF SURGEONS IN IRELAND (RCSI), PIC 999867368, established in ST STEPHEN'S GREEN 123, DUBLIN 2, Ireland,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

RIGAS STRADINA UNIVERSITATE (RSU), PIC 999843118, established in Dzirciema street 16, RIGA 1007, Latvia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

SCIENSANO (Sciensano), PIC 906160809, established in JULIETTE WYTSMANSTRAAT 14, ELSENE 1050, Belgium,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

SERVICE PUBLIC DE WALLONIE (SPW), PIC 999811884, established in Place de la Wallonie 1, Namur 5100, Belgium,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

SIGMUND FREUD PRIVATUNIVERSITAT WIEN GMBH (SFU), PIC 996709824, established in FREUDPLATZ 1, WIEN 1020, Austria,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

SIHTASUTUS EESTI TEADUSAGENTUUR (ETAg), PIC 998483760, established in SOOLA 8, TARTU 51004, Estonia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

SLOVENSKA AKADEMIA VIED (SAS), PIC 999530390, established in STEFANIKOVA 49, BRATISLAVA 814 38, Slovakia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

SONIO (Sonio), PIC 886915427, established in 24 RUE DU FAUBOURG SAINT-JACQUES, PARIS 75014, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

SOTSIAALMINISTEERIUM (MOSAE), PIC 998429731, established in Suur-Ameerika 1, TALLINN 10122, Estonia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

VETENSKAPSRADET - SWEDISH RESEARCH COUNCIL (SRC), PIC 999586165, established in BOX 1035, STOCKHOLM 101 38, Sweden,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

TEDDY - EUROPEAN NETWORK OF EXCELLENCE FOR PAEDIATRIC CLINICAL RESEARCH (TEDDY), PIC 910591963, established in VIA LUIGI PORTA 14, PAVIA 231261, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

TEKKARE (TEKKARE), PIC 881967069, established in 11-19 RUE DE LA VANNE, SOPARQ, BAT C, MONTROUGE 92120, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

THALASSAEMIA INTERNATIONAL FEDERATION (TIF), PIC 940669626, established in AKROPOLEOS 21 STROVOLOS, LEFKOSIA 2006, Cyprus,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

TURKIYE BILIMSEL VE TEKNOLOJIK ARASTIRMA KURUMU (TUBITAK), PIC 999587135, established in Ataturk Bulvari 221, ANKARA 06100, Türkiye,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

REGIONE TOSCANA (RT (TuscReg)), PIC 998823842, established in Palazzo Strozzi Sacrati - Piazza del Duomo 10, FIRENZE 50122, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITAT AUTONOMA DE BARCELONA (UAB), PIC 999986484, established in EDIF A CAMPUS DE LA UAB BELLATERRA CERDANYOLA V, CERDANYOLA DEL VALLES 08193, Spain,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITY COLLEGE DUBLIN, NATIONAL UNIVERSITY OF IRELAND, DUBLIN (UCD), PIC 999974359, established in BELFIELD, DUBLIN 4, Ireland,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITA CATTOLICA DEL SACRO CUORE (UCSC), PIC 999915771, established in LARGO GEMELLI 1, MILANO 20123, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ITA-SUOMEN YLIOPISTO (UEF), PIC 991207984, established in YLIOPISTONRANTA 8, KUOPIO 70211, Finland,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITAETSKLINIKUM AACHEN (UKA), PIC 999897632, established in Pauwelsstrasse 30, AACHEN 52074, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITAETSKLINIKUM FREIBURG (UKLFR), PIC 999881918, established in HUGSTETTER STRASSE 49, FREIBURG 79106, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITA DEGLI STUDI DELLA CAMPANIA LUIGI VANVITELLI (UNICAMPANIA), PIC 999848356, established in VIALE ABRAMO LINCOLN 5, CASERTA 81100, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

PANEPISTIMIO KRITIS (UoC), PIC 999588978, established in UNIVERSITY CAMPUS GALLOS, RETHIMNO 74100, Greece,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITEIT GENT (UGENT), PIC 999986096, established in SINT PIETERSNIEUWSTRAAT 25, GENT 9000, Belgium,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERZITETNI KLINICNI CENTER LJUBLJANA (UKCL), PIC 999882306, established in ZALOSKA CESTA 002, LJUBLJANA 1000, Slovenia,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

STICHTING WORLD DUCHENNE ORGANIZATION (WDO), PIC 930321860, established in KONINGINNELAAN 69, VEENENDAAL 3905 GG, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UPPSALA UNIVERSITET (UU), PIC 999985029, established in VON KRAEMERS ALLE 4, UPPSALA 751 05, Sweden,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CONECT4CHILDREN STICHTING (c4c-S), PIC 881618063, established in NICOLAAS BEETSSTRAAT 216, UTRECHT 3511 HG, Netherlands,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITE CADI AYYAD (CAU), PIC 998639930, established in BOULEVARD ABDELKARIM KHATTABI, MARRAKECH 40 000, Morocco,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE CNRS (CNRS), PIC 999997930, established in RUE MICHEL ANGE 3, PARIS 75794, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CONSORCIO CENTRO DE INVESTIGACION BIOMEDICA EN RED M.P. (CIBER), PIC 997154957, established in CALLE MONFORTE DE LEMOS 5, MADRID 28029, Spain,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNITATEA EXECUTIVA PENTRU FINANTAREA INVATAMANTULUI SUPERIOR A CERCETARII DEZVOLTARII SI INOVARII (UEFISCDI), PIC 972130024, established in STR D I MENDELEEV 21-25, BUCURESTI 010362, Romania,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITA DEGLI STUDI DI ROMA LA SAPIENZA (UNIROMA1), PIC 999987745, established in Piazzale Aldo Moro 5, ROMA 00185, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITEIT ANTWERPEN (UANTWERPEN), PIC 999902870, established in PRINSSTRAAT 13, ANTWERPEN 2000, Belgium,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

BULGARIAN NATIONAL SCIENCE FUND (BNSF), PIC 984222335, established in BLVD KNYAZ DONDUKOV 2 A, SOFIA 1000, Bulgaria,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

REGION NORDJYLLAND (NORTH DENMARK REGION) (Aalborg UH), PIC 997381064, established in Niels Bohrs Vej 30, AALBORG 9220, Denmark,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

REDKI BOLESTI BULGARIA (RDB), PIC 880694720, established in NISHAVA 121, SOFIA 1408, Bulgaria,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

BIOBANKS AND BIOMOLECULAR RESOURCES RESEARCH INFRASTRUCTURE CONSORTIUM (BBMRI-ERIC) (BBMRI-ERIC), PIC 946597878, established in NEUE STIFTINGTALSTRASSE 2/B/6, GRAZ 8010, Austria,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

AARHUS UNIVERSITETSHOSPITAL (AarhusUH), PIC 999643880, established in PALLE JUUL-JENSENS BOULEVARD 99, AARHUS 8200, Denmark,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ASSOCIATION INTERNATIONALE DE STANDARDISATION BIOLOGIQUE POUR L'EUROPE(IABS-EU) (IABS-EU), PIC 934774936, established in 24 RUE JEAN BALDASSINI, LYON 69393, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

HEALTH RESEARCH CHARITIES IRELAND COMPANY LIMITED BY GUARANTEE (HRCI), PIC 880683274, established in 12 CAMDEN ROW, DUBLIN D08 R9CN, Ireland,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

LUDWIG-MAXIMILIANS-UNIVERSITAET MUENCHEN (LMU), PIC 999978433, established in GESCHWISTER SCHOLL PLATZ 1, MUNCHEN 80539, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

MYSCIENCEWORK (MSW), PIC 898132119, established in 101 RUE DE SEVRES LOT 1674, PARIS 75006, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FONDS NATIONAL DE LA RECHERCHE (FNR), PIC 998597153, established in 2 AVENUE DE L'UNIVERSITE, ESCH-SUR-ALZETTE 4365, Luxembourg,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

NEMZETI KUTATASI FEJLESZTESI ES INNOVACIOS HIVATAL (NKFIH), PIC 999578696, established in KETHLY ANNA TER 1, BUDAPEST 1077, Hungary,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

BUNDESINSTITUT FUR IMPFSTOFFE UND BIOMEDIZINISCHE ARZNEIMITTEL (PEI), PIC 998217301, established in PAUL-EHRLICH-STRASSE 51-59, LANGEN 63225, Germany,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

PARIS-LODRON-UNIVERSITAT SALZBURG (PLUS), PIC 999868047, established in KAPITELGASSE 4-6, SALZBURG 5020, Austria,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

SORBONNE UNIVERSITE (SU), PIC 909875521, established in 21 RUE DE L'ECOLE DE MEDECINE, PARIS 75006, France,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITA DEGLI STUDI DI SIENA (UNISI), PIC 999898020, established in VIA BANCHI DI SOTTO 55, SIENA 53100, Italy,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

VERKET FOR INNOVATIONSSYSTEM (Vinnova), PIC 999618757, established in MASTER SAMUELSG 56, STOCKHOLM 10158, Sweden,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FUNDACIO CENTRE DE REGULACIO GENOMICA (CRG-CERCA), PIC 999544455, established in CARRER DOCTOR AIGUADER 88, BARCELONA 08003, Spain,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

REGION SKANE (GMS-RS), PIC 998165794, established in REGION SKANE, KRISTIANSTAD 291 89, Sweden,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

VIB VZW (VIB), PIC 999651931, established in SUZANNE TASSIERSTRAAT 1, ZWIJNAARDE - GENT 9052, Belgium,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTITUT DE PATHOLOGIE ET DE GENETIQUE ASBL (IPG), PIC 878266034, established in Av. Georges Lemaitre 25, GOSSELIES 6041, Belgium,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITY OF OTAGO (UO), PIC 998331567, established in SAINT DAVID STREET, DUNEDIN 9054, New Zealand,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

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SIGNATURE

For the beneficiary

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ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

HOSPITAL SANT JOAN DE DEU (HSJD), PIC 997929890, established in PASEO SANT JOAN DE DEU 2, ESPLUGUES DE LLOBREGAT 08950, Spain,

hereby agrees

to become beneficiary

in Agreement No 101156595 — ERDERA ('the Agreement')

between INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM) **and** the **European Health and Digital Executive Agency (HADEA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

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SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2024)5602406 - 02/08/2024

FINANCIAL STATEMENT FOR [PARTICIPANT NAME] FOR REPORTING PERIOD [NUMBER]

	Eligible[1] costs (per budget category)																	EU contribution[2]				Revenues
	Direct costs															Indirect costs	Total costs	EU contribution to eligible costs			Total requested EU contribution	Income generated by the action
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories								E. Indirect costs[2]		Funding rate %[3]	Maximum EU contribution[4]	Requested EU contribution		
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	[D.1 Financial support to third parties]	D.2 Internally invoiced goods and services	[D.3 Transnational access to research infrastructure unit costs]	[D.4 Virtual access to research infrastructure unit costs]	*[OPTION for HE PCP/PPI:* D.5 PCP/PPI procurement costs*]*	*[OPTION for Euratom Programme Cofund Actions:* D.6 Euratom Cofund staff mobility costs*]*	*[OPTION for HE ERC Grants:* D.7 ERC additional funding*]*	*[OPTION for HE ERC Grants:* D.8 ERC additional funding (subcontracting, FSTP and internally invoiced goods and services)*]*	E. Indirect costs						
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[5]	Actual costs	Actual costs	Actual costs	Actual costs	[Actual costs]	Unit costs (usual accounting practices)	[Unit costs[5]]	[Unit costs[5]]	[Actual costs]	[Unit costs[5]]	[Actual costs]	[Actual costs]	Flat-rate costs[6]						
	a1	a2	a3	b	c1	c2	c3	[d1a]	d2	[d3]	[d4]	[d5]	[d6]	[d7]	[d8]	e = 0,25 * (a1 + a2 + a3 ~~+b+~~ c1 +c2 + c3 ~~+d1a + d2 + d3 + d4 [+ d5][+ d6]~~ [+d7] ~~[+ d8]~~)	f = a+b+c+d+e	U	g = f*U%	h	m	n
XX – [short name beneficiary/affiliated entity]																						

The beneficiary/affiliated entity hereby confirms that:

The information provided is complete, reliable and true.

The costs and contributions declared are eligible (see Article 6).

The costs and contributions can be substantiated by adequate records and supporting documentation that will be produced upon request or in the context of checks, reviews, audits and investigations (see Articles 19, 20 and 25).

For the last reporting period: that all the revenues have been declared (see Article 22).

① Please declare all eligible costs and contributions, even if they exceed the amounts indicated in the estimated budget (see Annex 2). Only amounts that were declared in your individual financial statements can be taken into account lateron, in order to replace costs/contributions that are found to be ineligible.

[1] See Article 6 for the eligibility conditions. All amounts must be expressed in EUR (see Article 21 for the conversion rules).

[2] If you have also received an EU operating grant during this reporting period, you cannot claim indirect costs - unless you can demonstrate that the operating grant does not cover any costs of the action. This requires specific accounting tools. Please contact us immediately via the Funding & Tenders Portal for details.

[3] See Data Sheet for the reimbursement rate(s).

[4] This is the *theoretical* amount of EU contribution to costs that the system calculates automatically (by multiplying the reimbursement rates by the costs declared). The amount you request (in the column 'requested EU contribution') may be less.

[5] See Annex 2a 'Additional information on the estimated budget' for the details (units, cost per unit).

[6] See Data Sheet for the flat-rate.

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ANNEX 5

SPECIFIC RULES

CONFIDENTIALITY AND SECURITY (— ARTICLE 13)

Sensitive information with security recommendation

Sensitive information with a security recommendation must comply with the additional requirements imposed by the granting authority.

Before starting the action tasks concerned, the beneficiaries must have obtained all approvals or other mandatory documents needed for implementing the task. The documents must be kept on file and be submitted upon request by the coordinator to the granting authority. If they are not in English, they must be submitted together with an English summary.

For requirements restricting disclosure or dissemination, the information must be handled in accordance with the recommendation and may be disclosed or disseminated only after written approval from the granting authority.

EU classified information

If EU classified information is used or generated by the action, it must be treated in accordance with the security classification guide (SCG) and security aspect letter (SAL) set out in Annex 1 and Decision 2015/444[1] and its implementing rules — until it is declassified.

Deliverables which contain EU classified information must be submitted according to special procedures agreed with the granting authority.

Action tasks involving EU classified information may be subcontracted only with prior explicit written approval from the granting authority and only to entities established in an EU Member State or in a non-EU country with a security of information agreement with the EU (or an administrative arrangement with the Commission).

EU classified information may not be disclosed to any third party (including participants involved in the action implementation) without prior explicit written approval from the granting authority.

ETHICS (— ARTICLE 14)

Ethics and research integrity

The beneficiaries must carry out the action in compliance with:

- ethical principles (including the highest standards of research integrity)

[1] Commission Decision 2015/444/EC, Euratom of 13 March 2015 on the security rules for protecting EU classified information (OJ L 72, 17.3.2015, p. 53).

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and

- applicable EU, international and national law, including the EU Charter of Fundamental Rights and the European Convention for the Protection of Human Rights and Fundamental Freedoms and its Supplementary Protocols.

No funding can be granted, within or outside the EU, for activities that are prohibited in all Member States. No funding can be granted in a Member State for an activity which is forbidden in that Member State.

The beneficiaries must pay particular attention to the principle of proportionality, the right to privacy, the right to the protection of personal data, the right to the physical and mental integrity of persons, the right to non-discrimination, the need to ensure protection of the environment and high levels of human health protection.

The beneficiaries must ensure that the activities under the action have an exclusive focus on civil applications.

The beneficiaries must ensure that the activities under the action do not:

- aim at human cloning for reproductive purposes
- intend to modify the genetic heritage of human beings which could make such modifications heritable (with the exception of research relating to cancer treatment of the gonads, which may be financed)
- intend to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer, or
- lead to the destruction of human embryos (for example, for obtaining stem cells).

Activities involving research on human embryos or human embryonic stem cells may be carried out only if:

- they are set out in Annex 1 or
- the coordinator has obtained explicit approval (in writing) from the granting authority.

In addition, the beneficiaries must respect the fundamental principle of research integrity — as set out in the European Code of Conduct for Research Integrity[2].

This implies compliance with the following principles:

- reliability in ensuring the quality of research reflected in the design, the methodology, the analysis and the use of resources
- honesty in developing, undertaking, reviewing, reporting and communicating research in a transparent, fair and unbiased way

[2] European Code of Conduct for Research Integrity of ALLEA (All European Academies).

- respect for colleagues, research participants, society, ecosystems, cultural heritage and the environment

- accountability for the research from idea to publication, for its management and organisation, for training, supervision and mentoring, and for its wider impacts

and means that beneficiaries must ensure that persons carrying out research tasks follow the good research practices including ensuring, where possible, openness, reproducibility and traceability and refrain from the research integrity violations described in the Code.

Activities raising ethical issues must comply with the additional requirements formulated by the ethics panels (including after checks, reviews or audits; see Article 25).

Before starting an action task raising ethical issues, the beneficiaries must have obtained all approvals or other mandatory documents needed for implementing the task, notably from any (national or local) ethics committee or other bodies such as data protection authorities.

The documents must be kept on file and be submitted upon request by the coordinator to the granting authority. If they are not in English, they must be submitted together with an English summary, which shows that the documents cover the action tasks in question and includes the conclusions of the committee or authority concerned (if any).

VALUES (— ARTICLE 14)

Gender mainstreaming

The beneficiaries must take all measures to promote equal opportunities between men and women in the implementation of the action and, where applicable, in line with the gender equality plan. They must aim, to the extent possible, for a gender balance at all levels of personnel assigned to the action, including at supervisory and managerial level.

INTELLECTUAL PROPERTY RIGHTS (IPR) — BACKGROUND AND RESULTS — ACCESS RIGHTS AND RIGHTS OF USE (— ARTICLE 16)

Definitions

Access rights — Rights to use results or background.

Dissemination — The public disclosure of the results by appropriate means, other than resulting from protecting or exploiting the results, including by scientific publications in any medium.

Exploit(ation) — The use of results in further research and innovation activities other than those covered by the action concerned, including among other things, commercial exploitation such as developing, creating, manufacturing and marketing a product or process, creating and providing a service, or in standardisation activities.

Fair and reasonable conditions — Appropriate conditions, including possible financial terms or royalty-free conditions, taking into account the specific circumstances of the request for access, for example the actual or potential value of the results or background to which access is requested and/or the scope, duration or other characteristics of the exploitation envisaged.

FAIR principles — ‘findability’, ‘accessibility’, ‘interoperability’ and ‘reusability’.

Open access — Online access to research outputs provided free of charge to the end-user.

Open science — An approach to the scientific process based on open cooperative work, tools and diffusing knowledge.

Research data management — The process within the research lifecycle that includes the organisation, storage, preservation, security, quality assurance, allocation of persistent identifiers (PIDs) and rules and procedures for sharing of data including licensing.

Research outputs — Results to which access can be given in the form of scientific publications, data or other engineered results and processes such as software, algorithms, protocols, models, workflows and electronic notebooks.

Scope of the obligations

For this section, references to ‘beneficiary’ or ‘beneficiaries’ do not include affiliated entities (if any).

Agreement on background

The beneficiaries must identify in a written agreement the background as needed for implementing the action or for exploiting its results.

Where the call conditions restrict control due to strategic interests reasons, background that is subject to control or other restrictions by a country (or entity from a country) which is not one of the eligible countries or target countries set out in the call conditions and that impact the exploitation of the results (i.e. would make the exploitation of the results subject to control or restrictions) must not be used and must be explicitly excluded from it in the agreement on background — unless otherwise agreed with the granting authority.

Ownership of results

Results are owned by the beneficiaries that generate them.

However, two or more beneficiaries own results jointly if:

- they have jointly generated them and
- it is not possible to:
  - establish the respective contribution of each beneficiary, or
  - separate them for the purpose of applying for, obtaining or maintaining their protection.

The joint owners must agree — in writing — on the allocation and terms of exercise of their joint ownership (‘**joint ownership agreement**’), to ensure compliance with their obligations under this Agreement.

Unless otherwise agreed in the joint ownership agreement or consortium agreement, each joint owner may grant non-exclusive licences to third parties to exploit the jointly-owned results (without any right to sub-license), if the other joint owners are given:

- at least 45 days advance notice and
- fair and reasonable compensation.

The joint owners may agree — in writing — to apply another regime than joint ownership.

If third parties (including employees and other personnel) may claim rights to the results, the beneficiary concerned must ensure that those rights can be exercised in a manner compatible with its obligations under the Agreement.

The beneficiaries must indicate the owner(s) of the results (results ownership list) in the final periodic report.

Protection of results

Beneficiaries which have received funding under the grant must adequately protect their results — for an appropriate period and with appropriate territorial coverage — if protection is possible and justified, taking into account all relevant considerations, including the prospects for commercial exploitation, the legitimate interests of the other beneficiaries and any other legitimate interests.

Exploitation of results

Beneficiaries which have received funding under the grant must — up to four years after the end of the action (see Data Sheet, Point 1) — use their best efforts to exploit their results directly or to have them exploited indirectly by another entity, in particular through transfer or licensing.

If, despite a beneficiary's best efforts, the results are not exploited within one year after the end of the action, the beneficiaries must (unless otherwise agreed in writing with the granting authority) use the Horizon Results Platform to find interested parties to exploit the results.

If results are incorporated in a standard, the beneficiaries must (unless otherwise agreed with the granting authority or unless it is impossible) ask the standardisation body to include the funding statement (see Article 17) in (information related to) the standard.

Additional exploitation obligations

Where the call conditions impose additional exploitation obligations (including obligations linked to the restriction of participation or control due to strategic assets, interests, autonomy or security reasons), the beneficiaries must comply with them — up to four years after the end of the action (see Data Sheet, Point 1).

Where the call conditions impose additional exploitation obligations in case of a public emergency, the beneficiaries must (if requested by the granting authority) grant for a limited period of time specified in the request, non-exclusive licences — under fair and reasonable conditions — to their results to legal entities that need the results to address the public emergency and commit to rapidly and broadly exploit the resulting products and services at fair and reasonable conditions. This provision applies up to four years after the end of the action (see Data Sheet, Point 1).

Additional information obligation relating to standards

Where the call conditions impose additional information obligations relating to possible standardisation, the beneficiaries must — up to four years after the end of the action (see Data Sheet, Point 1) — inform the granting authority, if the results could reasonably be expected to contribute to European or international standards.

Transfer and licensing of results

Transfer of ownership

The beneficiaries may transfer ownership of their results, provided this does not affect compliance with their obligations under the Agreement.

The beneficiaries must ensure that their obligations under the Agreement regarding their results are passed on to the new owner and that this new owner has the obligation to pass them on in any subsequent transfer.

Moreover, they must inform the other beneficiaries with access rights of the transfer at least 45 days in advance (or less if agreed in writing), unless agreed otherwise in writing for specifically identified third parties including affiliated entities or unless impossible under the applicable law. This notification must include sufficient information on the new owner to enable the beneficiaries concerned to assess the effects on their access rights. The beneficiaries may object within 30 days of receiving notification (or less if agreed in writing), if they can show that the transfer would adversely affect their access rights. In this case, the transfer may not take place until agreement has been reached between the beneficiaries concerned.

Granting licences

The beneficiaries may grant licences to their results (or otherwise give the right to exploit them), including on an exclusive basis, provided this does not affect compliance with their obligations.

Exclusive licences for results may be granted only if all the other beneficiaries concerned have waived their access rights.

Granting authority right to object to transfers or licensing — Horizon Europe actions

Where the call conditions in Horizon Europe actions provide for the right to object to transfers or licensing, the granting authority may — up to four years after the end of the action (see Data Sheet, Point 1) — object to a transfer of ownership or the exclusive licensing of results, if:

- the beneficiaries which generated the results have received funding under the grant
- it is to a legal entity established in a non-EU country not associated with Horizon Europe, and
- the granting authority considers that the transfer or licence is not in line with EU interests.

Beneficiaries that intend to transfer ownership or grant an exclusive licence must formally notify the granting authority before the intended transfer or licensing takes place and:

- identify the specific results concerned
- describe in detail the new owner or licensee and the planned or potential exploitation of the results, and
- include a reasoned assessment of the likely impact of the transfer or licence on EU interests, in particular regarding competitiveness as well as consistency with ethical principles and security considerations.

The granting authority may request additional information.

If the granting authority decides to object to a transfer or exclusive licence, it must formally notify the beneficiary concerned within 60 days of receiving notification (or any additional information it has requested).

No transfer or licensing may take place in the following cases:

- pending the granting authority decision, within the period set out above
- if the granting authority objects
- until the conditions are complied with, if the granting authority objection comes with conditions.

A beneficiary may formally notify a request to waive the right to object regarding intended transfers or grants to a specifically identified third party, if measures safeguarding EU interests are in place. If the granting authority agrees, it will formally notify the beneficiary concerned within 60 days of receiving notification (or any additional information requested).

Granting authority right to object to transfers or licensing — Euratom actions

Where the call conditions in Euratom actions provide for the right to object to transfers or licensing, the granting authority may — up to four years after the end of the action (see Data Sheet, Point 1) — object to a transfer of ownership or the exclusive or non-exclusive licensing of results, if:

- the beneficiaries which generated the results have received funding under the grant
- it is to a legal entity established in a non-EU country not associated to the Euratom Research and Training Programme 2021-2025 and
- the granting authority considers that the transfer or licence is not in line with the EU interests.

Beneficiaries that intend to transfer ownership or grant a licence must formally notify the granting authority before the intended transfer or licensing takes place and:

- identify the specific results concerned
- describe in detail the results, the new owner or licensee and the planned or potential exploitation of the results, and
- include a reasoned assessment of the likely impact of the transfer or licence on EU interests, in particular regarding competitiveness as well as consistency with

ethical principles and security considerations (including the defence interests of the EU Member States under Article 24 of the Euratom Treaty).

The granting authority may request additional information.

If the granting authority decides to object to a transfer or licence, it will formally notify the beneficiary concerned within 60 days of receiving notification (or any additional information requested).

No transfer or licensing may take place in the following cases:

- pending the granting authority decision, within the period set out above
- if the granting authority objects
- until the conditions are complied with, if the granting authority objection comes with conditions.

A beneficiary may formally notify a request to waive the right to object regarding intended transfers or grants to a specifically identified third party, if measures safeguarding EU interests are in place. If the granting authority agrees, it will formally notify the beneficiary concerned within 60 days of receiving notification (or any additional information requested).

Limitations to transfers and licensing due to strategic assets, interests, autonomy or security reasons of the EU and its Member States

Where the call conditions restrict participation or control due to strategic assets, interests, autonomy or security reasons, the beneficiaries may not transfer ownership of their results or grant licences to third parties which are established in countries which are not eligible countries or target countries set out in the call conditions (or, if applicable, are controlled by such countries or entities from such countries) — unless they have requested and received prior approval by the granting authority.

The request must:

- identify the specific results concerned
- describe in detail the new owner and the planned or potential exploitation of the results, and
- include a reasoned assessment of the likely impact of the transfer or license on the strategic assets, interests, autonomy or security of the EU and its Member States.

The granting authority may request additional information.

Access rights to results and background

Exercise of access rights — Waiving of access rights — No sub-licensing

Requests to exercise access rights and the waiver of access rights must be in writing.

Unless agreed otherwise in writing with the beneficiary granting access, access rights do not include the right to sub-license.

If a beneficiary is no longer involved in the action, this does not affect its obligations to grant access.

If a beneficiary defaults on its obligations, the beneficiaries may agree that that beneficiary no longer has access rights.

Access rights for implementing the action

The beneficiaries must grant each other access — on a royalty-free basis — to background needed to implement their own tasks under the action, unless the beneficiary that holds the background has — before acceding to the Agreement —:

- informed the other beneficiaries that access to its background is subject to restrictions, or

- agreed with the other beneficiaries that access would not be on a royalty-free basis.

The beneficiaries must grant each other access — on a royalty-free basis — to results needed for implementing their own tasks under the action.

Access rights for exploiting the results

The beneficiaries must grant each other access — under fair and reasonable conditions — to results needed for exploiting their results.

The beneficiaries must grant each other access — under fair and reasonable conditions — to background needed for exploiting their results, unless the beneficiary that holds the background has — before acceding to the Agreement — informed the other beneficiaries that access to its background is subject to restrictions.

Requests for access must be made — unless agreed otherwise in writing — up to one year after the end of the action (see Data Sheet, Point 1).

Access rights for entities under the same control

Unless agreed otherwise in writing by the beneficiaries, access to results and, subject to the restrictions referred to above (if any), background must also be granted — under fair and reasonable conditions — to entities that:

- are established in an EU Member State or Horizon Europe associated country

- are under the direct or indirect control of another beneficiary, or under the same direct or indirect control as that beneficiary, or directly or indirectly controlling that beneficiary and

- need the access to exploit the results of that beneficiary.

Unless agreed otherwise in writing, such requests for access must be made by the entity directly to the beneficiary concerned.

Requests for access must be made — unless agreed otherwise in writing — up to one year after the end of the action (see Data Sheet, Point 1).

Access rights for the granting authority, EU institutions, bodies, offices or agencies and national authorities to results for policy purposes — Horizon Europe actions

In Horizon Europe actions, the beneficiaries which have received funding under the grant must grant access to their results — on a royalty-free basis — to the granting authority, EU institutions, bodies, offices or agencies for developing, implementing and monitoring EU policies or programmes. Such access rights do not extend to beneficiaries' background.

Such access rights are limited to non-commercial and non-competitive use.

For actions under the cluster 'Civil Security for Society', such access rights also extend to national authorities of EU Member States for developing, implementing and monitoring their policies or programmes in this area. In this case, access is subject to a bilateral agreement to define specific conditions ensuring that:

- the access rights will be used only for the intended purpose and
- appropriate confidentiality obligations are in place.

Moreover, the requesting national authority or EU institution, body, office or agency (including the granting authority) must inform all other national authorities of such a request.

Access rights for the granting authority, Euratom institutions, funding bodies or the Joint Undertaking Fusion for Energy — Euratom actions

In Euratom actions, the beneficiaries which have received funding under the grant must grant access to their results — on a royalty-free basis — to the granting authority, Euratom institutions, funding bodies or the Joint Undertaking Fusion for Energy for developing, implementing and monitoring Euratom policies and programmes or for compliance with obligations assumed through international cooperation with non-EU countries and international organisations.

Such access rights include the right to authorise third parties to use the results in public procurement and the right to sub-license and are limited to non-commercial and non-competitive use.

Additional access rights

Where the call conditions impose additional access rights, the beneficiaries must comply with them.

COMMUNICATION, DISSEMINATION, OPEN SCIENCE AND VISIBILITY (— ARTICLE 17)

Dissemination

Dissemination of results

The beneficiaries must disseminate their results as soon as feasible, in a publicly available format, subject to any restrictions due to the protection of intellectual property, security rules or legitimate interests.

A beneficiary that intends to disseminate its results must give at least 15 days advance notice to the other beneficiaries (unless agreed otherwise), together with sufficient information on the results it will disseminate.

Any other beneficiary may object within (unless agreed otherwise) 15 days of receiving notification, if it can show that its legitimate interests in relation to the results or background would be significantly harmed. In such cases, the results may not be disseminated unless appropriate steps are taken to safeguard those interests.

Additional dissemination obligations

Where the call conditions impose additional dissemination obligations, the beneficiaries must also comply with those.

Open Science

Open science: open access to scientific publications

The beneficiaries must ensure open access to peer-reviewed scientific publications relating to their results. In particular, they must ensure that:

- at the latest at the time of publication, a machine-readable electronic copy of the published version or the final peer-reviewed manuscript accepted for publication, is deposited in a trusted repository for scientific publications

- immediate open access is provided to the deposited publication via the repository, under the latest available version of the Creative Commons Attribution International Public Licence (CC BY) or a licence with equivalent rights; for monographs and other long-text formats, the licence may exclude commercial uses and derivative works (e.g. CC BY-NC, CC BY-ND) and

- information is given via the repository about any research output or any other tools and instruments needed to validate the conclusions of the scientific publication.

Beneficiaries (or authors) must retain sufficient intellectual property rights to comply with the open access requirements.

Metadata of deposited publications must be open under a Creative Common Public Domain Dedication (CC 0) or equivalent, in line with the FAIR principles (in particular machine-actionable) and provide information at least about the following: publication (author(s), title, date of publication, publication venue); Horizon Europe or Euratom funding; grant project name, acronym and number; licensing terms; persistent identifiers for the publication, the authors involved in the action and, if possible, for their organisations and the grant. Where applicable, the metadata must include persistent identifiers for any research output or any other tools and instruments needed to validate the conclusions of the publication.

Only publication fees in full open access venues for peer-reviewed scientific publications are eligible for reimbursement.

Open science: research data management

The beneficiaries must manage the digital research data generated in the action (‘data’) responsibly, in line with the FAIR principles and by taking all of the following actions:

- establish a data management plan (‘DMP’) (and regularly update it)

- as soon as possible and within the deadlines set out in the DMP, deposit the data in a trusted repository; if required in the call conditions, this repository must be federated in the EOSC in compliance with EOSC requirements

- as soon as possible and within the deadlines set out in the DMP, ensure open access — via the repository — to the deposited data, under the latest available version of the Creative Commons Attribution International Public License (CC BY) or Creative Commons Public Domain Dedication (CC 0) or a licence with equivalent rights, following the principle 'as open as possible as closed as necessary', unless providing open access would in particular:

    - be against the beneficiary's legitimate interests, including regarding commercial exploitation, or

    - be contrary to any other constraints, in particular the EU competitive interests or the beneficiary's obligations under this Agreement; if open access is not provided (to some or all data), this must be justified in the DMP

- provide information via the repository about any research output or any other tools and instruments needed to re-use or validate the data.

Metadata of deposited data must be open under a Creative Common Public Domain Dedication (CC 0) or equivalent (to the extent legitimate interests or constraints are safeguarded), in line with the FAIR principles (in particular machine-actionable) and provide information at least about the following: datasets (description, date of deposit, author(s), venue and embargo); Horizon Europe or Euratom funding; grant project name, acronym and number; licensing terms; persistent identifiers for the dataset, the authors involved in the action, and, if possible, for their organisations and the grant. Where applicable, the metadata must include persistent identifiers for related publications and other research outputs.

Open science: additional practices

Where the call conditions impose additional obligations regarding open science practices, the beneficiaries must also comply with those.

Where the call conditions impose additional obligations regarding the validation of scientific publications, the beneficiaries must provide (digital or physical) access to data or other results needed for validation of the conclusions of scientific publications, to the extent that their legitimate interests or constraints are safeguarded (and unless they already provided the (open) access at publication).

Where the call conditions impose additional open science obligations in case of a public emergency, the beneficiaries must (if requested by the granting authority) immediately deposit any research output in a repository and provide open access to it under a CC BY licence, a Public Domain Dedication (CC 0) or equivalent. As an exception, if the access would be against the beneficiaries' legitimate interests, the beneficiaries must grant non-exclusive licenses — under fair and reasonable conditions — to legal entities that need the research output to address the public emergency and commit to rapidly and broadly exploit the resulting products and services at fair and reasonable conditions. This provision applies up to four years after the end of the action (see Data Sheet, Point 1).

Plan for the exploitation and dissemination of results including communication activities

Unless excluded by the call conditions, the beneficiaries must provide and regularly update a plan for the exploitation and dissemination of results including communication activities.

SPECIFIC RULES FOR CARRYING OUT THE ACTION (— ARTICLE 18)

Implementation in case of restrictions due to strategic assets, interests, autonomy or security of the EU and its Member States

Where the call conditions restrict participation or control due to strategic assets, interests, autonomy or security, the beneficiaries must ensure that none of the entities that participate as affiliated entities, associated partners, subcontractors or recipients of financial support to third parties are established in countries which are not eligible countries or target countries set out in the call conditions (or, if applicable, are controlled by such countries or entities from such countries) — unless otherwise agreed with the granting authority.

The beneficiaries must moreover ensure that any cooperation with entities established in countries which are not eligible countries or target countries set out in the call conditions (or, if applicable, are controlled by such countries or entities from such countries) does not affect the strategic assets, interests, autonomy or security of the EU and its Member States.

Recruitment and working conditions for researchers

The beneficiaries must take all measures to implement the principles set out in the Commission Recommendation on the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers[3], in particular regarding:

- working conditions
- transparent recruitment processes based on merit, and
- career development.

The beneficiaries must ensure that researchers and all participants involved in the action are aware of them.

Specific rules for access to research infrastructure activities

Definitions

Research Infrastructures — Facilities that provide resources and services for the research communities to conduct research and foster innovation in their fields. This definition includes the associated human resources, and it covers major equipment or sets of instruments; knowledge-related facilities such as collections, archives or scientific data infrastructures; computing systems, communication networks, and any other infrastructure, of a unique nature and open to external users, essential to achieve excellence in research and innovation. Where relevant, they may be used beyond research, for example

[3] Commission Recommendation 2005/251/EC of 11 March 2005 on the European Charter for Researchers and on a Code of Conduct for the Recruitment of Researchers (OJ L 75, 22.3.2005, p. 67).

for education or public services, and they may be 'single-sited', 'virtual' or 'distributed'[4]:

When implementing access to research infrastructure activities, the beneficiaries must respect the following conditions:

- for transnational access:
  - access which must be provided:

    The access must be free of charge, transnational access to research infrastructure or installations for selected user-groups.

    The access must include the logistical, technological and scientific support and the specific training that is usually provided to external researchers using the infrastructure. Transnational access can be either in person (hands-on), provided to selected users that visit the installation to make use of it, or remote, through the provision to selected user-groups of remote scientific services (e.g. provision of reference materials or samples, remote access to a high-performance computing facility).

  - categories of users that may have access:

    Transnational access must be provided to selected user-groups, i.e. teams of one or more researchers (users).

    The majority of the users must work in a country other than the country(ies) where the installation is located (unless access is provided by an international organisation, the Joint Research Centre (JRC), an ERIC or similar legal entity).

    Only user groups that are allowed to disseminate the results they have generated under the action may benefit from the access (unless the users are working for SMEs).

    Access for user groups with a majority of users not working in a EU Member State or Horizon Europe associated country is limited to 20% of the total amount of units of access provided under the grant (unless a higher percentage is foreseen in Annex 1).

  - procedure and criteria for selecting user groups:

    The user groups must request access by submitting (in writing) a description of the work that they wish to carry out and the names, nationalities and home institutions of the users.

    The user groups must be selected by (one or more) selection panels set up by the consortium.

[4] See Article 2(1) of the Horizon Europe Framework Programme Regulation 2021/695.

The selection panels must be composed of international experts in the field, at least half of them independent from the consortium (unless otherwise specified in Annex 1).

The selection panels must assess all proposals received and recommend a short-list of the user groups that should benefit from access.

The selection panels must base their selection on scientific merit, taking into account that priority should be given to user groups composed of users who:

- have not previously used the installation and
- are working in countries where no equivalent research infrastructure exist.

It will apply the principles of transparency, fairness and impartiality.

Where the call conditions impose additional rules for the selection of user groups, the beneficiaries must also comply with those.

- other conditions:

The beneficiaries must request written approval from the granting authority for the selection of user groups requiring visits to the installations exceeding 3 months (unless such visits are foreseen in Annex 1).

In addition, the beneficiaries must:

- advertise widely, including on a their websites, the access offered under the Agreement
- promote equal opportunities in advertising the access and take into account the gender dimension when defining the support provided to users
- ensure that users comply with the terms and conditions of the Agreement
- ensure that its obligations under Articles 12, 13, 17 and 33 also apply to the users
- keep records of the names, nationalities, and home institutions of users, as well as the nature and quantity of access provided to them

- for virtual access:
  - access which must be provided:

The access must be free of charge, virtual access to research infrastructure or installations.

'Virtual access' means open and free access through communication networks to digital resources and services needed for research, without selecting the users to whom access is provided.

The access must include the support that is usually provided to external users.

Where allowed by the call conditions, beneficiaries may in justified cases define objective eligibility criteria (e.g. affiliation to a research or academic institution) for specific users.

- other conditions:

  The beneficiaries must have the virtual access services assessed periodically by a board composed of international experts in the field, at least half of whom must be independent from the consortium (unless otherwise specified in Annex 1). For this purpose, information and statistics on the users and the nature and quantity of the access provided, must be made available to the board.

  The beneficiaries must advertise widely, including on a dedicated website, the access offered under the grant and the eligibility criteria, if any.

  Where the call conditions impose additional traceability[5] obligations, information on the traceability of the users and the nature and quantity of access must be provided by the beneficiaries.

These obligations apply regardless of the form of funding or budget categories used to declare the costs (unit costs or actual costs or a combination of the two).

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Specific rules for Co-funded Partnerships

When implementing financial support to third parties in Co-funded Partnerships, the beneficiaries must respect the following conditions:

- avoid any conflict of interest and comply with the principles of transparency, non-discrimination and sound financial management
- for the types of activity and categories of persons that will be supported:
  - for multi-beneficiary projects (including multi-participant projects): the projects supported must be transnational, involving at least two independent legal entities from two different EU Member States or Horizon Europe associated countries as recipients of the financial support and may also include legal entities established in a non-associated third countries not receiving financial support
  - for mono-beneficiary projects (multi-participant projects): the projects supported must be transnational, involving one legal entity established in an EU Member State or Horizon Europe associated country as recipient of the financial support and one legal entity established in a non-associated third country not receiving financial support
- for the selection procedure and criteria:

[5] According to the definition given in ISO 9000, i.e.: “Traceability is the ability to trace the history, application, use and location of an item or its characteristics through recorded identification data.” The users can be traced, for example, by authentication and/or by authorization or by other means that allows for analysis of the type of users and the nature and quantity of access provided.

- publish open calls widely (including on the Funding & Tenders Portal and the beneficiaries' websites)
- keep open calls open for at least two months
- inform recipients of call updates (if any) and the outcome of the call (list of selected projects, amounts and names of selected recipients)
- measures to avoid potential conflicts of interest or unequal treatment of applicants must be ensured (notably through appropriate communication/exchange of information channels and independent and fair complaints procedures)
- use the following selection criteria: the standard Horizon Europe award criteria
- use the following selection procedures:
    - projects must be selected following a joint transnational call for proposals
    - beneficiaries must make the selection through a two-step procedure:
        - Step 1: review at national or transnational level (including national eligibility checks)
        - Step 2: single international peer review

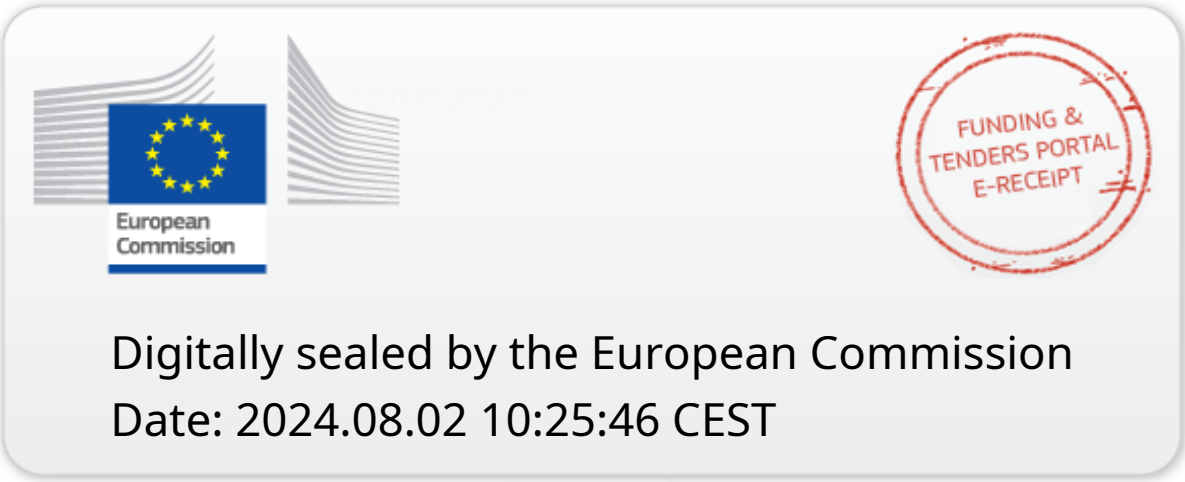
      and in Step 2:

        - proposals must be evaluated with the assistance of at least three independent experts
        - proposals must be ranked according to the evaluation results and the selection must be made on the basis of this ranking
        - the selection procedure must be followed by an independent expert observer, who must make a report.

Where the financial support is implemented through implementing partners, the beneficiaries must:

- ensure that the partners comply with the same rules, standards and procedures for implementing the financial support
- implement effective monitoring and oversight arrangements towards the partners, covering all aspects relating to the action
- ensure effective and reliable reporting by the partners, covering the activities implemented, information on indicators, as well as the legality and regularity of the expenditure claimed
- ensure that the partners provide that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the final recipients

where the call conditions restrict participation or control due to strategic assets, interests, autonomy or security reasons: apply the restrictions set out in Annex 5 mutatis mutandis to the final recipients and their results.



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