HORIZON-HLTH-2022-DISEASE-06-04-two-stage:

Development of new effective therapies for rare diseases (RIA)

Subsidy: €8M
Funding rate: 100%
Deadline: First stage: 1 February 2022
Second stage: 6 September 2022
Duration: No limit; up to 4 years is recommended
Total budget: €60M

Consortium:

At least three legal entities established in different Member States or Associated Countries.

The involvement of patient representatives in all phases of the research and development process is strongly encouraged.

Scope

Despite the considerable amount of knowledge that has been accumulated and the new orphan medicines developed in recent years, the number of available therapies for rare diseases remains low, as fewer than 6% of rare diseases have an approved treatment option.

The joint evaluation[1] of the regulations on orphan medicinal products and paediatric medicines concluded that those regulations have boosted the development for new therapies for rare diseases but have not yet adequately managed to direct research and innovation in areas of greatest unmet medical need. Actually, there is an urgent unmet medical need for the development of therapies for rare diseases, where there is still no approved therapeutic option available.

Therefore, proposals should aim to develop therapies for rare diseases with no approved therapeutic option. Proposals should focus on group(s) of rare diseases with commonalities, such as shared biological features, possibly within the same and/or

[1] https://ec.europa.eu/health/sites/health/files/files/paediatrics/docs/orphan-regulation_eval_swd_2020-163_part-3.pdf

across different medical areas within the rare diseases landscape[2]. Thus, proposals should not address a single disease only (for example with an Orphacode representing a single disease).

The therapies to be developed may include a broad family of therapeutic interventions such as small molecule(s), advanced therapy medicinal products, repurposing of existing medicinal products, including non-pharmacological interventions and/or their combinations, as relevant. Sex and gender aspects should be considered, where relevant. To ensure that the needs of people living with a rare disease are adequately addressed, the involvement of patient representatives in all phases of the research and development process is strongly encouraged. Rare infectious diseases and rare cancers are excluded from this topic and will not be considered.

The topic will support proposals covering several different stages in the continuum of the innovation pathway (i.e. translational, preclinical, clinical research, validation in the clinical and/or real-world setting etc.), as relevant. SME(s) participation is encouraged with the aim to strengthen the scientific and technological basis of SME(s) and valorise their innovations for the benefit of people living with a rare disease.

The proposals should address most of the following research activities:

- Establish multidisciplinary collaborations between all relevant stakeholders by integrating disciplines, technological developments and existing knowledge. Integrate harmonised data from multiple sources (i.e. natural history studies/clinical trials, multi-omics, medical imaging, registries etc.) by utilising data analytics and/or other suitable methods, with the aim to understand the pathophysiology/heterogeneity of the rare diseases concerned and to identify therapeutically actionable mechanisms.
- Develop and utilise relevant preclinical models and/or innovative tools/technologies to: verify molecular/cellular pathways/genes that can be therapeutically targeted, increase the confidence in the targets selection and/or perform toxicity studies. When using disease models the applicants should describe how well the model replicates the pathology or the human condition.
- Develop and/or execute innovative clinical trials designs for small populations and novel approaches to assess and monitor the safety and efficacy of the proposed interventions. Such approaches may include but are not limited to: biomarkers defining robust surrogate and clinical endpoints; artificial intelligence tools/medical devices/biosensors/companion/complementary diagnostics for defining reliable patient reported outcomes; modelling and simulation and in-silico trials methodologies.

[2] Medical areas such as: neurology, immunology, dermatology, endocrinology-metabolism etc. - see EMA therapeutic areas: https://www.ema.europa.eu/en/human-regulatory/researchdevelopment/prime-priority-medicine

- Carry out preclinical proof-of-concept (PoC) studies and/or multinational interventional clinical studies[3] to demonstrate the safety and efficacy of the therapeutic interventions under study. Preclinical PoC studies should include late-stage preclinical studies (i.e. toxicological properties, adverse effects etc.). Clinical studies may cover all necessary development stages. Applicants should propose a clear exploitation pathway through the different necessary steps (research, manufacturing, regulatory approvals and licensing, IP management etc.) in order to accelerate marketing authorisation and uptake by the health systems.

Expected Outcome

This topic aims at supporting activities that are enabling or contributing to one or several expected impacts of destination 3 "Tackling diseases and reducing disease burden". To that end, proposals under this topic should aim for delivering results that are directed, tailored towards and contributing to some of the following expected outcomes:

- Researchers and developers make the best use of the state-of-the-art knowledge and resources for a fast and effective development of new therapies for rare diseases.
- Researchers and developers increase the development success rate of therapies for rare diseases by employing robust preclinical models, methods, technologies, validated biomarkers, reliable patient reported outcomes and/or innovative clinical trials designs.
- Developers and regulators move faster towards market approval of new therapies for rare diseases (with currently no approved treatment option) due to an increased number of interventions successfully tested in late stages of clinical development.
- Healthcare professionals and people living with a rare disease get access to new therapeutic interventions and/or orphan medicinal products.

Additional Information

Proposals should involve group(s) of rare diseases (i.e. a rare disease being individually defined in the European Union as affecting not more than five in 10.000 persons). Proposals that plan to run clinical trials should demonstrate that they have already

[3] Template for providing essential information in proposals involving clinical studies https://ec.europa.eu/research/participants/data/ref/h2020/other/legal/templ/h2020_tmpl-clinical-studies_2018-2020_en.pdf

taken into account scientific advice or protocol assistance from EMA. In particular, proposals planning the clinical development of orphan medicinal products should demonstrate that they have been granted approval for an orphan designation at the latest on the date of the call deadline.

Proposals should adhere to the FAIR[4] data principles and take stock, wherever relevant, of data standards, harmonisation guidelines and good practices for data sharing/access developed by existing European health research infrastructures (i.e. ESFRI infrastructures[5]). Proposals should take stock, where relevant, of the FAIR guidance, of good practices for analytical methods and preclinical models and of good exploitation strategies for the translation of research results into high impact interventions, developed by the European Joint Programme on Rare Diseases[6] (EJP RD) and other relevant EU-funded projects. Whenever the proposed data sources or fields of application include genomics, the proposals should take into account, where relevant, the data standards, and legal, ethical and technical interoperability requirements and guidelines agreed within the 1+ Million Genomes initiative[7]. Data-intensive proposals, particularly those using data from patient registries, could consider the involvement of the European Commission's Joint Research Centre (JRC) and take stock of the tools and services provided by the European Platform on Rare Disease Registration (EU RD Platform), including the adoption, where relevant, of the European standards such as the "set of common data elements"[8]. In addition, synergies should be sought with the European Reference Networks[9], where relevant.

Projects funded under this topic will contribute towards the goals of the International Rare Diseases Research Consortium (IRDiRC) that supports the development of 1000 new therapies for rare diseases by 2027 and may take stock of the IRDiRC Orphan Drug Development Guidebook[10], where relevant.

[4] FAIR data are data, which meet principles of findability, accessibility, interoperability, and reusability.
[5] 2018 Roadmap of the European Strategy Forum on Research Infrastructures (ESFRI) with list of ESFRI research infrastructures (pp 15-17), https://ec.europa.eu/info/sites/info/files/research_and_innovation/esfri-roadmap-2018.pdf.
[6] https://www.ejprarediseases.org/
[7] https://digital-strategy.ec.europa.eu/en/policies/1-million-genomes
[8] https://eu-rd-platform.jrc.ec.europa.eu/set-of-common-data-elements_en
[9] https://ec.europa.eu/health/ern_en
[10] https://irdirc.org/orphan-drug-development-guidebook-materials/