All information regarding future IHI Call topics is indicative and subject to change. Final information about future IHI Calls will be communicated after approval by the IHI Governing Board.

Topic 4: Strengthening the European ecosystem for Advanced Therapy Medicinal Products (ATMPs) and other innovative therapeutic modalities for rare diseases

Expected impacts to be achieved by this topic

- Patients with rare diseases, especially underserved rare diseases, benefit from an increased availability of effective and safe ATMPs and other innovative therapeutic modalities.
- The development of ATMPs and other innovative therapeutic modalities for rare disorders (which are frequently genetically defined) will be streamlined thanks to enhanced scientific and technological processes.
- Europe becomes more attractive for developing ATMPs thanks to the availability of sustained, interconnected technological centres of excellence that could be linked to and would benefit from the activities of clinical networks, including the European Reference Networks (ERNs) on rare diseases. This would provide a more efficient and effective path for the development of therapies for patients with rare diseases.
- Although focused on rare diseases, the ability of centres of excellence to improve the development of ATMPs and other innovative therapeutic modalities is anticipated to benefit a broader range of diseases beyond rare diseases.

Expected outcomes

Research and innovation (R&I) actions to be supported under this topic must contribute to all the following outcomes:

- A sustainable network of interconnected centres of excellence with all relevant stakeholders engaged, that should:
    i. be accessible by all involved in the development of ATMPs and other innovative therapeutic modalities, including the research community, academia, clinics, small to medium-sized enterprises (SMEs), healthcare, biotech, medical technology and pharmaceutical companies, patient organisations,
    ii. represent the most promising, impactful, translatable, quality-controlled technologies that facilitate the development of ATMPs and other innovative therapeutic modalities such as use of nucleic acids and nanoparticle (NPs) delivery for gene editing.
- Agreed standards that support the early generation of ATMPs and other innovative therapeutic modalities.
- A streamlined and more transparent regulatory pathway to optimise and speed up the development and delivery of ATMPs and other innovative therapeutic modalities for rare diseases for the benefit of patients, carers, healthcare systems and the society.

- Improved technologies/processes, analytic tools, methods, assays useful for the development and support of all ATMPs and other innovative therapeutic modalities, beyond those targeting underserved rare diseases.

Scope

There are over 7000 rare diseases resulting in 30 million patients[1] in Europe with a rare disease. Globally more than 300 million patients[2] are affected. In Europe, less than 10% of rare disease patients receive treatment and only 1% are managed using an approved treatment. There are many challenges in the development of treatments for rare diseases, notably Advanced Therapy Medicinal Products (ATMPs) and other innovative therapeutic modalities, such as gene and cell therapies. They have shown promise yet rely on complex technologies with largely underdeveloped manufacturing processes.

The aim of this topic is to optimise and streamline the development of ATMPs and other innovative therapeutic modalities for rare diseases by strengthening the ecosystem that facilitates the transition of early research to development. This will streamline and improve the value chain of advanced therapies from bench to market.

To fulfil this aim, the selected projects should:

1. Establish a network of interconnected and complimentary scientific and technical centres of excellence (de novo and/or existing laboratories/institutions) in defined types of ATMPs or other innovative therapeutic modalities to enable translational research. This covers therapeutic approaches relevant to the future treatment of genetically defined diseases. The scientific and technical centres are expected to provide access and advance translatable, quality-controlled technologies. These centres should develop technologies and share data, and to provide an opportunity to define key characteristics of ATMPs, and quality standards that are critical to later stage development. Relevant therapeutic modalities include recombinant adeno-associated virus (rAAV), and innovative modalities such as messenger RNA (mRNA) and nanoparticles (NPs) for therapeutics. Technology areas of interest include targeted delivery, stability, transgene expression, advanced redosing technology approaches/reduced immunogenicity of gene delivery platforms, and other underlying biology relevant to the specific therapeutic modality, enabling accelerated translation to clinical development and manufacturing.

2. Develop standardised analytical assays, methods and technological platforms, and design strategies for

    i. reducing the timeframe and costs and improve the robust assessment of therapeutic modalities and/or;

    ii. optimising of advanced manufacturing processes to assure product quality, ensuring broad accessibility of critical manufacturing materials and demonstrating the economy of scale for ATMPs or other innovative therapeutic modalities.

3. Demonstrate the translatability, scalability, and robustness of technologies suitable for the development of subsequent ATMPs and other innovative therapeutic modalities. This may include process development, mRNA and NPs scale up and stability, vector production, improvement of the throughput capability for the systematic assessment of the biological and mechanistic features and product characterisation, and ensuring broad accessibility of critical manufacturing materials such as cell lines and producer plasmids.

[1] https://www.eurordis.org/information-support/what-is-a-rare-disease/
[2] https://www.nature.com/articles/s41431-019-0508-0

4. Implement use cases in defined types of ATMPs, representing groups of rare diseases with commonalities, with the aim of demonstrating the performance of the methods and technologies developed for addressing the bottlenecks in the development and manufacturing cycles of ATMPs and other therapeutic modalities.

5. Assess the methods and technological platforms developed for their regulatory validity/utility. Define a regulatory pathway to support the fit-for purpose development of ATMPs, taking into account an evolving regulatory environment and the interplay between all applicable legislation. Engage early with the regulators to ensure that the methods and data generated support regulatory needs.

6. Contribute to strengthening the European rare disease ecosystem by ensuring the engagement of all relevant stakeholders, especially patients and patients' representatives for rare diseases, carers, clinicians, regulators.

7. Define metrics to measure the use of centres of excellence by relevant stakeholders for the development of their assets or novel technological solutions/therapies.

This topic focuses on the scientific and technological barriers that are limiting the rapid and cost-effective development of ATMPs and other innovative therapeutic modalities for underserved rare disease patients. To test the functionality of the centres of excellence, the utility of the processes developed and whether they are fit-for purpose, ATMPs may be used for proof of concept. Nonetheless the development of ATMPs and/or clinical trials are out of scope for this topic.

Applicant consortia should take stock of the state-of-the-art methods and technologies delivered by other inter-connecting EU and global initiatives (e.g., Bespoke, IMI project ARDAT, or other EU funded consortia) and their proposals should reflect potential synergies and collaborations to ensure complementarity while avoiding duplication.

Why the expected outcomes can only be achieved by an IHI project

A cross-sectorial and multidisciplinary public-private collaboration driving innovative science and technology solutions is needed to deliver on the outcomes and impacts of this topic, fostering a trusted collaborative environment where the end-users integrate from day one with the innovation developers to ensure projects generate useful and usable outputs that will be sustained for longer term impact. There is a need to remove key technical bottlenecks, facilitate collaboration and co-operation and bring together all relevant stakeholders in order to streamline the translation of early research into development of potential ATMPs. This will enable accessibility to world leading solutions that would otherwise limit or delay progression through development and towards effective treatment for patients. Therefore, collaboration and synergies between the research institutions, clinics who often conduct the early research and biotech, SMEs, pharma as well as med tech companies is critical to ensure that the approached can be translated. Bringing on board the unique expertise of patients and advocates in rare diseases in this effort is essential. Early engagement with regulators is fundamental to maximise the impact of these technologies on public health and ensure they are fit for purpose. Finally, connection with clinicians and rare diseases networks are needed to ensure an integrated development pathway for ATMPs for rare diseases.

Indicative budget

IHI estimates that an IHI financial contribution of around EUR 20 000 000 to 30 000 000 would allow a proposal to address these outcomes appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts. ***NB: this amount is indicative and subject to change, pending approval by the IHI Governing Board.***

Applicant consortia must ensure that at least 45% of the action's eligible costs are provided by contributions from industry members, their constituent or affiliated entities, and contributing partners.

Additional Activities from industry members and their constituent or affiliated entities may also contribute towards this 45% threshold, providing these activities are related to the project. Contributing partners do not contribute additional activities.

Indicative duration of the actions

Applicants should propose a project duration that matches the project's activities and expected outcomes and impacts.

Dissemination and exploitation obligations

[To be determined: The specific obligations described in the Conditions of the calls and calls management rules under "Specific conditions on availability, accessibility and affordability" [apply][do not apply][3].]

[3] See section 4.2.3.2 of this amended Work Programme