

**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 translational research ecosystem for advanced therapy medicinal products (ATMPs) for rare diseases**

### **Expected impacts to be achieved by this topic**

- Benefits for patients both with rare and ultra-rare diseases and who may gain from effective and safe advanced therapy medicinal products (ATMPs) and other related innovative therapeutic modalities.
- A better and more cost-effective development of ATMPs and other related innovative therapeutic modalities due to improved scientific and technological processes. This is applicable especially to those ATMPs intended both for the treatment of rare diseases and those that are currently underserved by current therapies (the latter often being of genetic origin).
- Europe to become more attractive for developing ATMPs due to the availability of sustained, interconnected networks of technological and scientific centres of excellence. Although their current focus is on translational research, linkages to clinical networks, including the European reference networks (ERNs) on rare diseases will enhance their activities. The same is true for synergies to be developed with the European Joint Programme on Rare Diseases and the future European partnership on rare diseases. This would set out a more efficient and effective pathway for the development of treatment modalities for patients with rare diseases in Europe.
- Benefits for a broader range of disorders beyond the rare disease domain due to a more robust development of ATMPs and other related innovative therapeutic modalities as well as knowledge transfer across actors in ATMP development.

### **Expected outcomes**

Research and innovation (R&I) actions to be supported under this topic must work towards results that contribute to all the following expected outcomes.

- A sustainable network of centres of excellence, that should:
  - i. advance the most promising, impactful, translatable, quality-controlled technologies that address the bottlenecks in the development of ATMPs and other related innovative therapeutic modalities such as the use of messenger RNA (mRNA), or nucleic acids and nanoparticle (NPs) delivery for gene editing;
  - ii. make these technologies accessible to all actors involved in the development of ATMPs and other related innovative therapeutic modalities, including the research community, academia, clinics, small to medium-sized enterprises (SMEs), healthcare professionals, biotech, medical technology and pharmaceutical companies, and patients;
  - iii. share information, processes and methods, and build capacity in science and technology, and regulatory awareness of ATMPs, including the ability to assist industrial and academic developers of ATMPs in their translational research.

- Consensus reached on quality standards (e.g. of analytical methods) and translation process by the ATMP community at large that support the timely and robust development of ATMPs and other related innovative therapeutic modalities.
- Strengthened interactions with regulators to enable a more streamlined and transparent regulatory pathway that will 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 society.
- Improved technologies/processes, analytic tools, methods including non-clinical methods, and assays useful for the development of ATMPs and other related innovative therapeutic modalities, beyond those targeting rare and ultra-rare diseases.

## Scope

There are over 7 000 rare diseases resulting in 30 million patients<sup>1</sup> in Europe with a rare disease. Globally more than 300 million patients<sup>2</sup> are affected. In Europe, less than 10 % of rare disease patients receive treatment and only 1 % are managed using an approved treatment. ATMPs such as gene and cell therapies and other related innovative therapeutic modalities, are very promising to treat patients with rare diseases, especially ultra-rare diseases. However, ATMPs rely on complex technologies where the development process is hampered by a lack of standardisation, scalability and reproducibility.

The overall aim of this topic is to optimise and streamline the future development of ATMPs and other related innovative therapeutic modalities for rare diseases by strengthening the ecosystem that facilitates the transition of early pre-clinical proof-of-concept research to clinical development. This topic focuses on the scientific, technological and regulatory barriers that are limiting translational research into rapid and cost-effective development of ATMPs and other related innovative therapeutic modalities for rare diseases.

To fulfil this aim, the proposals should:

1. Establish a network of scientific and technical centres of excellence (new and/or existing laboratories/institutions) complementing each other to enable translational research in ATMPs or other related innovative therapeutic modalities relevant to the future treatment of genetically defined diseases. These scientific and technical centres are expected to provide access and advance translatable, quality-controlled technologies, share data, and build capacity to assist industrial and academic developers of ATMPs. They are also expected to explore the establishment of connections with clinical networks, including the ERNs on rare diseases.
2. Develop tools and methods and define key characteristics of ATMPs, and quality standards that are critical to later stages of development of ATMPs and other related innovative therapeutic modalities, in particular those targeting rare diseases with no approved treatment option. Relevant therapeutic modalities must include appropriate vector systems and innovative modalities such as messenger RNA (mRNA) and nanoparticles (NPs) for therapeutics. Technology areas of interest could include targeted delivery (e.g. methods to target distribution), stability (e.g. methods to increase the stability of RNA), 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.

<sup>1</sup> <https://www.eurordis.org/information-support/what-is-a-rare-disease/>

<sup>2</sup> <https://www.nature.com/articles/s41431-019-0508-0>

3. Develop and support the uptake of standardised analytical assays, methods and technological platforms, other non-clinical methods and design strategies as well as translation processes for:
  - i. reducing the timeframe and costs and improving the future development of ATMPs and other related innovative therapeutic modalities and/or;
  - ii. optimising manufacturing processes to maintain product quality while ensuring broad accessibility of critical manufacturing materials and demonstrating the economy of scale for ATMPs or other related innovative therapeutic modalities.
4. Demonstrate the translatability, scalability, and robustness of technologies suitable for the development of subsequent ATMPs and other related innovative therapeutic modalities. This may include process development, mRNA and NPs scale-up and stability, vector production, increasing the throughput of 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.
5. Assess the methods and technological platforms developed for their translational and 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. Ensure early engagement with the regulators so that the methods and data generated support regulatory needs.
6. Validate the performance of the methods and technologies developed and demonstrate their higher performance in comparison to existing methods for addressing the bottlenecks in the development and manufacturing cycles of ATMPs and other related innovative therapeutic modalities. In addition, test the functionality of the centres of excellence and demonstrate their capability and performance to support translational research through use cases.

To achieve this, the submitted proposals must plan for an open expression of interest / call process to invite third parties, external to the initially established consortium, to submit use cases at least twice during the lifetime of the project. These use cases must:

  - i. showcase the utility and validity of the methods and technologies developed and verify that they are fit for purpose in the context of the scientific, technological or regulatory challenges; and
  - ii. measure and help adjust the capability and performance of centres and networks of excellence in assisting industrial and academic developers of ATMPs in their translational research.

For the use cases, clinical validation of technological solutions developed would be in the scope of this topic (within the framework of the above objectives). While conducting full randomised controlled trials are out of scope for this topic, other forms of clinical studies are in scope under the use cases, which may include pilot clinical studies, observational studies, real world data studies etc., depending on the needs of proponents of the use cases.

7. Contribute to strengthening the European rare disease ecosystem by engaging all relevant stakeholders, especially patients and patients' representatives for rare diseases, carers, clinicians, and regulators.
8. Define relevant metrics and measure the use of centres of excellence by relevant stakeholders for the development of their assets or novel technological solutions/therapies.
9. Define a plan for sustainability beyond the lifetime of the project, including consideration for potential expansion to additional promising technological areas.

Applicant consortia should take stock of the state-of-the-art methods and technologies delivered by other EU and global initiatives on rare diseases (e.g. the Accelerating Medicines Partnership Bespoke Gene Therapy

Consortium, the Innovative Medicines Initiative (IMI) project ARDAT, the European Joint Programme on Rare Diseases and the future European partnership on rare diseases, or other EU-funded consortia). Proposals should plan for 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 cooperation and sharing information and processes 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, pharmaceutical and medical technology companies is critical to ensure that the approaches 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 maximising the impact of these technologies on public health and ensuring they are fit for purpose. Finally, connections with clinicians and rare diseases networks are needed to ensure an integrated development pathway for ATMPs for rare diseases.

### **Indicative budget**

Applicant consortia will be competing for the maximum financial contribution from IHI up to EUR 30 000 000.

IHI estimates that an IHI financial contribution of between EUR 20 000 000 and EUR 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.

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**

The specific obligations described in the Conditions of the calls and calls management rules under "Specific conditions on availability, accessibility and affordability" apply<sup>3</sup>.

<sup>3</sup> See section 4.2.3.2 of this amended Work Programme.