Accelerating Research and Innovation for ATMPs (ARDAT)

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There is a need for Public-Private Collaboration in ATMP research and innovation

Context

- Lack of data that is important for ATMP development regarding host responses, persistence of efficacy, redosing, and safety.
- Expertise in gene and cell therapy lies in academia or is siloed across institutions and companies.
- Need to combine deep expertise and innovation in vector design, adeno-associated virus (AAV) biology, cell biology, and immunology from academia, with growing industry ATMP development expertise, data emerging from clinical trials, and regulatory expertise lying in regulatory agencies.

There is a need for Public-Private Collaboration in ATMP research and innovation

Project Objectives

- Develop better, standardized models for predicting product immunogenicity in humans.
- Build our understanding of gene/cell therapy drug metabolism within a host and explore any loss of efficacy (persistence), particularly with non-integrating viral vectors or cell therapy.
- Understand the clinical factors around pre-existing immunity limiting patient access to ATMP therapy, and adaptive immune responses affecting product safety, efficacy, and persistence.
- Engage regulators to ensure that the models and data generated through the funded action will provide the necessary information to support regulatory filings and to address regulatory, safety, and efficacy concerns.

Pre-competitive nature drives impact across the partnership

- Develop a general ATMP characterization framework that will benefit the field and is limited to the pre-competitive space.
- Understand aspects of gene / cell therapy without a particular disease focus.
- Utilize non-oncological rare disease models to accomplish the appropriate characterization.
- A coordinated effort to acquire and analyse the available ATMP data, and design preclinical and clinical studies to fill the knowledge gaps for the field.

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Pre-competitive nature drives impact across the partnership

- A data-driven development of a product-characterization framework to aid researchers, developers and regulators to more rapidly move effective, and safe gene/cell therapies forward to benefit patients in need.
- Joint efforts across pharma, biotech, academia, and regulatory functions will inform patient inclusion criteria, limit subtherapeutic dosing, and define the impact of the pre-existing and adaptive immunity on efficacy and persistence of gene/cell therapy.
- Help product developers and regulators to determine and implement an appropriate and effective characterization framework to enable efficient and safe development of gene/cell therapies.

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Proposed ‘work package’ project structure

WP1	WP2	WP3
• Management, co-ordination and dissemination	• Develop better, standardized models for predicting product immunogenicity in humans	• Build understanding of gene/cell therapy drug metabolism inside host • Explore loss of efficacy, esp. with non-integrating viral or non-viral vectors, or cell therapy

Applicants should indicate how their proposal will impact the competitiveness and industrial leadership of Europe.

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WP=Work Package

Proposed ‘work package’ project structure

WP4

- Understand clinical factors around pre-existing immunity limiting patient access to ATMPs
- Understand adaptive immune responses affecting product safety, efficacy and persistence, including for integrating vector-based therapies

WP5

- Engage regulators to ensure that the models and data generated through this project will provide the necessary information to support regulatory filings and to address regulatory and safety concerns

Applicants should indicate how their proposal will impact the competitiveness and industrial leadership of Europe.

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WP=Work Package

Expected contributions and experience of applicants to ensure project success

1 Research

- In R&D and regulation of ATMPs, with access to clinical cohorts and samples from patients dosed with gene or cell therapies.
- AAV biology, vectorology, production; drug delivery; tissue engineering; predictive organ-tissue models, in silico simulation, cell biology and production, transgenic animals, immunology, histology, omics, and in vivo experimentation.

2 Data

- State-of-the-art experience and expertise in the establishment of databases, data harmonisation, database management and data security

3 Regulatory

- In translating & conveying data for regulatory purposes.
- Regulatory bodies and bodies managing GMOs would bring important experience to the consortium 3

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The successful applicants will benefit in multiple areas

What to expect…

From In-Kind Consortium…

- **DATA:** Anonymised existing or prospective data from clinical trial cohorts from industry to supplement academic cohorts.
- **KNOWLEDGE**: Personnel with in-depth knowledge in the fields of experimental and clinical immunology, cell and in vivo biology, virology/vectorology, histology, genetic toxicology, omics, chemistry manufacturing & controls (CMC) analysis, medical affairs, statistics, regulatory, bioethics, epidemiology, and non-clinical development.
- **KNOW-HOW:** The means to support the establishment of the federated database including legal advice, setting up the database, making analysis feasible, accessible, and sustainable.

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What to expect…

For You…

- Access key data, industry insights & learnings for next generation of scientists; publication opportunities and fostering open scientific interaction in the public domain.
- SMEs focused in ATMP fields will have characterization data that can help development of their tools and methods.
- Patient organisations can provide perspectives, guidance and help facilitate providing medicine developers & regulators with the information needed to more safely and swiftly move transformative medicines to address patient need.
- Regulators will help guide evolution to a more data-driven characterization framework, rather than theoretically-based.

Key deliverables of the full project

- In vitro, ex vivo, and animal models with better translatability of the immune responses to gene/cell therapy that are sustainable.
- Deep understanding of how host cells and tissues metabolise gene/cell drug products and how this affects persistence.
- Identification of immunogenicity hurdles and potential solutions, for de-immunization or immunomodulation to improve efficacy and minimize patient risk along with a standardized vector characterization platform.

Key deliverables of the full project (cont)

- Standardised methods and gold standards to better characterize the products, such as potency, dose, and various quality properties.
- During Year 1, develop a plan for which issues will benefit the most from a comprehensive database(s) to address regulatory needs.
- Optimised and validated methods and models to increase regulatory acceptance and facilitate regulatory success of future gene therapy projects.
- A sustainable sample biobank from healthy volunteers / patients (with informed consent / privacy) treated with gene or cell therapies.

Thank you

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