

IMI consultation on advanced therapies

Response from the Spanish National Cancer Research Centre (CNIO)

To whom it may concern,

My name is Carolina Pola, PhD, and I am writing on behalf of the Spanish National Cancer Research Centre (CNIO) (Madrid, Spain) to submit our feedback and comments on the IMI Advanced Therapies Concept Paper. We hope our contribution will be helpful as the topic moves forward in IMI. This is an important area of translational research to be addressed by an important private-public collaborative initiative, such as IMI.

Please see below our comments. If you have any questions, please do not hesitate to contact me.

With kind regards,

Carolina

1. Have the key challenges that can be addressed through collaborative, public-private initiatives been properly identified?

Yes, they have. The concept paper is comprehensive and discusses the most relevant and pressing issues for the development of novel ATMPs. Nevertheless, we would like to underscore that preclinical models would benefit from having the expertise from public and private institutions, including research centers, universities, and companies specialized in animal models, especially large animals. A parallel initiative could be run as a working package of an international consortium to compare data obtained with more established animal models and human organoids to start implementing the latter in the development process and speed up data collection. Human organoids require specialization that may only be obtained at research centers where groups work with specific tissues and organoids. Knowledge on how to set up GLP or GMP that can be applied to human organoids is needed to use them as proper and valid models.

In addition, collaborative public-private initiatives will tackle the current problems derived from the limited or lack of investment by big pharma, which pushes translation to be achieved by start-ups or biotechs. This results in a substantial delay to reach the clinic. Moreover, there is a biased profile of ATMPs focused on genetic-based rare diseases. This leaves out other unmet medical needs such as Alzheimer's disease or Parkinson's diseases that are complex or polygenic genetic disorders.

2. Which of the proposed potential initiatives should be prioritized?

1) developing validated (by scientific evidence and regulatory agencies) model systems and vector types that can quickly be tested in humans for safety as well as other basic preclinical work (needed for ATMPs given its particular complex nature), and 2) defining the regulatory path for the different groups of ATMPs and the rational patient-selection criteria for each ATMPs-based approach (with a process that can start at the preclinical development to prevent derailing of promising preclinical progress).

3. Are any areas missing?

- Cross talk between preclinical and clinical teams (along with regulatory experts) would be ideal within the consortia to establish models at the preclinical stage that can recapitulate the patient selection and study design chosen for a clinical trial. This could facilitate that data and results in animals can better represent the clinical setting. Animal disease models should be as close as possible to the clinical situation.
- A relevant question could be how to implement these advanced therapies in the clinic, by exploring innovative ways of manufacturing and quality control that can be shared by industry and the medical center to lower prices and optimize delivery at the bedside. Perhaps the current model of manufacturing and preparation of the entire drug within the pharmaceutical industry should be questioned when it comes to gene and cell therapies. Perhaps setting "stations" or "pharma hubs"

within hospitals that can be used by trained hospital professionals to finish the product could be explored.

- Aside from aiming for a common generic vector, a future project should consider the tropism of vectors and the tissue targets, as a vector “one size fits all” may not be the most efficacious and safest option for some diseases. Preclinical development should address different vector types and a rational classification of vector that require integration versus those that do not integrate, depending on the needs of the disease. AAV-based gene therapy and its ability to establish long-term benefit through one intravenous administration could provide the basis for a potential commercially-viable gene therapy.
- Investment in out-of-the-box basic research, such as specific funding schemes for gene editing approaches, and building an efficient technology transfer and development platforms to integrate the advances in preclinical research into later stages (a highly integrated platform where all stakeholders are present to substantially contribute to generate novel products and shorten the time to reach the patient).

4. What are the key European or national initiatives that IMI shall synergize with?

- The European Alliance for Personalized Medicine <http://euapm.eu/> (to implement ATMPs in healthcare systems and facilitate pricing, reimbursement and access within different countries).
- Per Med <http://www.permed2020.eu/index.php>
- International Rare Diseases Research Consortium <http://www.irdirc.org/>
- International Cancer Genome Consortium <http://icgc.org/>
- Therapeutics for Rare and Neglected Diseases <http://www.ncats.nih.gov/trnd>

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