eatris

European infrastructure
for translational medicine

IMI ATMP CONSULTATION

The EATRIS ATMP platform aims to support development, from post-discovery to clinical proof of concept, of novel ATMP products. In doing so, we seek to identify the key issues which act as roadblocks in this development and to find solutions to optimize the translational pipeline for the development of these complex medicinal products to the patient. EATRIS has collated the opinions of our ATMP platform of experts (listed on pg 4) to consider the following questions outlined by this IMI consultation and to inform the IMI of the key areas that we feel have not been adequately addressed in a satisfactory manner and that currently represent gaps in the ATMP development field. Specifically:

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

➢ Most key challenges have been broadly addressed although focus is needed. Key challenges in all areas could be proactively addressed through initiatives utilizing research infrastructures. In addition, the activities identified are mostly in the reimbursement – legal framework for the hospital exemption and we agree that a better understanding of the current situation in all member states is necessary and urgent. Not all (academic) hospitals (f.i. Netherlands can get funding of their HE), which makes it hard to treat patient under HE. Payment by patient is in an academic setting not allowed. No funding.

➢ Other focus points should include collaborative projects between regulatory authorities and RIs on addressing specific issues in the manufacturing processes and product characterization and development. This amongst others should include decentralized, point of use manufacturing as an area that needs scientific, regulatory and legal clarification requesting the involvement of all relevant stakeholders.

➢ Standardization of manufacturing not only for purification but also for production processes should be addressed. This will facilitate generation of high quality vectors for gene transfer. Development of standards should be key to facilitate robustness and reproducibility, but also interpretation of data relevance.

- **Which of the proposed potential initiatives should be prioritised?**

➢ Addressing regulatory issues in ATMP development through funded projects

using the RIs where comparability across sites in multiple countries and institutions can be assessed. Close collaborative initiatives between the EMA, Academia and industry can address multiple bottlenecks in the translation of advanced therapies and assist the overall goal of streamlining development and moving ATMP development away from a cottage industry to a commercial one.

- ATMP developers need to formulate successful business plans many years prior to successfully bringing a product to market covering all aspects of development, regulatory, scale up and reimbursement. A harmonized approach to HTA and reimbursement policies would address this issue. A PPP initiative in this sense would substantially facilitate the development of ATMP in Europe.

- Transfer and scale up in manufacturing should be prioritized, as with the regulatory landscape becoming more clearer in ATMP development, the number of clinical trials and market approved products will start to increase. However it is of note that due to the nature of these products, if this product development cannot be transferred and scaled up in a commercial setting they will not be a viable clinical option as already evident by current approved ATMPs. Funding should be invested in the development of this transfer and scale up/scale out innovation (including bioreactors and modules), which should begin in parallel with the product's progress through the translational pipeline.

- The proposed initiatives outlined in this concept paper are important, but significant focus should be given to those at the beginning of the pipeline, that is those proposed in preclinical development. This should be followed by those on clinical development, then those on manufacturing, and finally finish by those affecting pricing and reimbursement.
  More specifically, among the different initiatives, we would prioritise:
  - Development of new relevant model systems and new enhanced vectors (Preclinical Development)
  - Identification of new biomarkers allowing preclinical to clinical translatability (Clinical Development)
  - Single confirmatory studies for safety and efficacy (Clinical Development)
  - Development of more efficient purification procedures and QC test of ATMPs (Manufacturing).

- **Are any areas missing?**

- There is little focus on standardization from the characterization of these ATMPs to the preclinical models to their eventual manufacture and scale up. This area

alone represents a pivotal need, which requires a consortium that should include RIs, regulators, and the manufacturers. This alone represents a standout need that can utilize historical data in ATMP development in creating a robust ATMP development process in each defined area.

- A precompetitive effort to define validated analytical tools regarding identity and potency assay are needed to speed up the ATMP development, as:
- Viral Safety of ATMPS - standardizing immunogenicity testing,
- Implementing alternatives to FBS
  This impacts on the Standardization/comparability with the Manufacturing Process transfer resulting in limited reproducibility between different sites-

- An automation of the manufacturing working to eliminate the human factor variability due to the operators and the related use of appropriate **personnel** in addition to product for heterogeneous, complex and individualized Production processes needs to be explored and defined

- The exploration of which models work best for which type of ATMP manufacturing- Centralized / decentralized / local (incl bedside) and the linked issue of distribution of cell therapy products from A-B as soon as a big clinical trial is approved. A discussion with reimbursement authority toward the movement of patients across Europe to be treated in specialized centres.

- **What are the key European or national initiatives that IMI shall synergise with?**

- Service providers as the Research Infrastructure EATRIS, ECRIN, INFRAFRONTIER
- European and National competent authorities (EMA, EDQM and member states)
- Scientific societies involved in academic development of ATMP like ISCT
- National infrastructures involved in ATMP development like ECELL (FR) and Cell and Gene CATAPULT (UK)
- Regulatory societies like EPSRC, NIBSC, GBSI, PDA or PIC

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