Overview of comments received on IMI Advanced Therapies Concept Paper

Stakeholder: CIBER-BBN

CIBER is a public Biomedical Research Networking Centre designed to be a translational research centre with a multidisciplinary and multiinstitutional nature made up of basic, clinical and technological research in a specific area for the purpose of developing a single common research programme, relevant for the Spanish National Health System.

CIBER is a consortium of research institutions, and belongs to the Instituto de Salud Carlos III (ISCIII, Carlos III Health Institute), responsible for coordination of biomedical research at the national level and attached to the Ministry of Economy of the Spanish government (MINECO).
The CIBER for Bioengineering, Biomaterials and Nanomedicine, CIBER-BBN, is dedicated by legal mandate to developing research (basic, clinical, epidemiological and healthcare services) and technological development activities, all related to the following descriptors: a) Telemedicine, b) Molecular imaging techniques in medicine, c) Tissue bioengineering, d) Nanostructures and drug release, e) Biocompatible nanoparticules, f) Biological nanosensors, g) Implantable nanomachines or nanorobots for biomedical diagnosis.

CIBER-BBN is currently formed by 45 core groups and 2 more associated groups, all belonging to a total of 27 institutions as universities, research centres, hospitals and technological centres. These groups were selected, by an international panel of experts, in a national call for proposals, based on their scientific production, international recognition and capacity to transfer their results to the biomedical field.

Interested parties (researchers of CIBER-BBN) that commented on the draft document as released for consultation.

Name Stakeholder	Institution
Margarita Calonge	Research Group on Ocular Surface Instituto Universitario de Oftalmobiología Aplicada – Universidad de Valladolid IOBA-UVA
Girish Kumar	Research Group on Retina IOBA-UVA
Ana Paula Candiota/ Carles Arús	Biomedical Applications of Magnetic Resonance research group Universitat Autònoma de Barcelona (UAB)
Iñaki Ochoa	Group of Structural Mechanics and Materials Modelling Universidad de Zaragoza (UNIZAR)
Simó Schwartz	CIBBIM-Nanomedicine. Drug Delivery and Targeting Group Vall d'Hebron Research Institute (VHIR) Coordinator of Technological Transfer Programme, CIBER-BBN
Ramón Martínez Máñez	Group of Releasing and Controlled Detention Universitat Politècnica de València (UPV) Scientific Director, CIBER-BBN

Questions of consultation

IMI and EFPIA are looking for input from scientific, regulatory, patient and healthcare systems communities on the following questions:

1. Have the key challenges that can be addressed through collaborative, public private initiatives been properly identified?
2. Which of the proposed potential initiatives should be prioritised?
3. Are any areas missing?
4. What are the key European or national initiatives that IMI shall synergise with?

General comments - overview

Researcher/Question	Comments and rationale/ proposed change
Margarita Calonge	
1	It is essential to have well defined animal models that are reliable, as close as possible to the human pathology and in which tolerance, safety and efficacy can be tested at the same time. An additional important benefit is to have in vitro systems involving the cell types affected where to test mechanisms of action, molecular characteristics, etc.
2	3.1 and 3.2 are critically important. There is still a lack of agreement about clinical criteria defining the potential inclusion or exclusion criteria for clinical trials as there is a lack of uniform definition of severity, grades, score systems. In ocular surface pathology, which stem cells damage leads to corneal blindness, the epidemiology (in terms of disease prevalence mainly) of the deficiency of stem cell deficiency is unknown. Some numbers given in some publications are only a wild guess. The reason is that stem cell deficiency is the end-stage of many different diseases.
3	-
4	It would be very useful and efficient to organize a European workshop with the mission of not leaving the meeting without establishing clear criteria about of the nebulous points, having designed work groups with a special task, whose results have to be presented in that workshop. Nothing of this could be done without economic compensation to the clinicians/investigators involved, as they would have to devote quite a lot of time to these tasks.

Researcher/Question	Comments and rationale/ proposed change
Girish Kumar	
1	Research approach to develop a treatment against a human disease needs appropriate testing systems representing pathological events which are initiated. Retina is the base for vision and has a big impact on life. Therefore, well characterised, stable in vitro models of retinal cells and tissues, and for follow-up test with animal models of retinal diseases are fundamental to target pathological events and its consequences in the retina and testing the tolerance, safety and efficacy of a treatment approach, and if it is close to human species and well regulated (GLP-like), transferring to clinical practice becomes easy and can occur in short period.
2	The pre-clinical (3.1) and clinical (3.2) research are well connected and equally important. Clinical study supports by clinical data to identify the targets in pathological conditions or treatment outcomes, and pre-clinical study proposes approaches to treat them. Although clinical study is crucial for evaluating safety, proof of concept and efficacy to reach up to product fabrication and comercialization stage but it is still deficient establishing uniform criteria in studies. There are reports showing success of stem cell application for the *Age-Related Macular Degeneration* (AMD) patients but none of them reach in daily clinical practice.
3	Industry supported consortiums very active in promoting multidisciplinary research. An active consortium with biomaterial research sector are crucial because many of treatment approaches in retina needs knoweldge in-puts from this sector. Similarly enforcing industry participation supports to quick transfer the successful treatment approach to market and in reach of millions of patients.
4	Frequent meetings is much needed at European and national level by inviting experts of different disciplines because it offers platform for to discuss and develop cooperation, however, productivity of such meetings must be under external evaluation annually to discard less productive groups.

Researcher/Question	Comments and rationale/ proposed change
Ana Paula Candiota/ Carles Arús	
1	Availability of enough ATMPs for preclinical studies (larger amounts would be needed in comparison with in vitro approaches). ATMPs synthesized under strict control quality standards and suitable for clinical use, which would be needed if clinical stage is reached. Development of better marketing and intellectual property strategies. Increase of the available funding for research expenses.
2	a) proposals with a high level of confidence and preliminary results (e.g. ATMPs assayed in small animals as mice and rats) with promising results; b) proposals related to illnesses/conditions with no or few strategies of cure or palliation; c) proposals in which ATMPs are synthesized under strict quality control conditions (e.g. in case of nanoparticles, they should be either LPS-free or to have LPS levels under the maximum allowed in ISO norms).
3	Specific linking areas, e.g. to specify parameters in the transition from in vitro to in vivo assays, or in vivo/in vivo assays (from small animals to larger animals). Help with the implementation of quality control directives in the academic field, to ensure proper coordination and complementation of the academic+private work.
4	Attempts of standardization of preclinical regulations, as well as a clear awareness campaign to inform citizens about the needs of preclinical studies in ATMPs research. Creation of a system to disseminate information about preclinical/clinical results obtained with new ATMPs, mainly addressed to other projects which are developing similar approaches, in order to benefit the enrolled patients.

Researcher/Question	Comments and rationale/ proposed change
Iñaki Ochoa	
1	Generation of in vitro humanized models based on microfluidic technologies (Organ on a chip). This part is aligned with the mentioned areas of interest and it is a bridge between areas 3.1 and 3.3. Reduction of animal experimentation and discovery of new therapeutic targets related with cellular microenvironment and/or the interaction between different cell types are some of the key aspects in which this technology could contribute. Moreover, using these in vitro models will allow to carry out some experiments which are not possible until now, and the time for the development of new related drugs will decrease (e.g. oncoimmunology)
2	It is necessary to develop new technologies in order to generate better preclinical models. With this the cost of clinical trials will decrease and the access to the market will be also faster. In this way, our prioritization is: manufacturing, preclinical development, clinical development and access to market.
3	The sample storage and sample preservation are very important aspects related with ATMPs. Many of the clinical applications which use ATMPs need a fast expansion, modification and differentiation of the cells in order to be suitable for the treatment.
4	It is necessary to have some funding initiatives involving big companies, SMEs, technological centers and Academia. A good approximation would be when a big company establishes some innovation lines, and afterwards works with SMEs and Academia research groups. European programs as IMI and Eurostar projects are good examples of this kind of partnership. At national level (Spain) the RETOS project is an adequate example of suitable public-private partnership, however the economic conditions are not very suitable for SMEs.

Researcher/Question	Comments and rationale/ proposed change
Simó Schwartz	
1	i. Definition of the TPP (Target Product Profile) considering the clinical needs (in this task researchers from Academia and Industry should work in a very close collaboration from the conception of the project) ii. Establishment of joint public-private commissions to contact regulatory agencies iii. Establishment of Academic GLP and GMP Units iv. Social acceptance of innovative therapies
2	i. Optimization of early preclinical studies and regulatory preclinical studies. Possibility of having suitable academic technological services to perform GLP studies ii. GMP manufacturing for preclinical and clinical studies iii. Clinical trials iv. Access to the market
3	i. Promotion of the interaction of Academia and Regulatory agencies from the conception of the innovative projects ii. Promotion of IPR and Business plans and Market studies. iii. Studies of clinical impact and collaboration with some Networks as EATRIS, ECRIN iv. Interaction with patients associations and more social dissemination of the projects outcomes
4	At national level (Spain) RETOS and CDTI projects are adequate examples of suitable public-private partnership, and IMI projects at international level.

Researcher/Question	Comments and rationale/ proposed change
Ramón Martínez Máñez	
1	Yes, we think key challenges have been properly identified. In particular, we agree with the complexity of the evaluation and standardization of that kind of products and the need of developing specific actions to facilitate the translation of ATMPs to the clinical practice.
2	We think manufacturing and preclinical development are the two pillars for a successful translation. With a robust base, clinical development would be achieved in a faster way and the product (and its solid scientific base) would attract easier to industrial partners.
3	Specially, we think it is necessary an extra effort on standardization. Mainly for nanomaterials, the creation of new characterization standards and a key characterization laboratory network would be of interest.
4	Clearly, fluent communication between academia and industrial partners is vital to succeed. The creation of i) more calls devoted to this kind of collaboration to stimulate industrial partners and ii) more workshops and networking events could help.

Report by:
Aída Castellanos Páez, PhD, MBA
R+D+i Project Manager
Biomaterials and Advanced Therapies Programme, CIBER-BBN
acastellanos@ciber-bbn.es

Coordinator of Biomaterials and Advanced Therapies Programme, CIBER-BBN:
Dr. Julio San Román
Institute of Polymer Science and Technology (ICTP)
Consejo Superior de Investigaciones Científicas (CSIC)