COLLABORATIVE PROJECTS – II Edition

Short version of the Call Text

Deadline: December 14th, 2018, 5 p.m.

Summary

BACKGROUND

The Lombardy Foundation for Biomedical Research (Fondazione Regionale per la Ricerca Biomedica FRRB) is an entity governed by public law, a non-for-profit organization, established in October 2011 by Regione Lombardia, with the aim of promoting and supporting scientific research in Life Sciences in Lombardy (since 2011, over 100 Million euros have been committed in innovative R&D projects). The Foundation represents the main strategic platform for boosting progress, research, development and innovation within the health sector among the regional academic and industrial life science players. Its *raison d'être* is to serve as support to and for implementing the regional health care research policy, in order to place the Lombardy regional system in a leading position in Europe within this field. In addition, the Foundation aims to distribute local and European resources to innovative basic and translational research projects, which enable a positive impact on the local health care eco-system and citizens.

FRRB, in accordance with Lombardy Region, is focusing its activity on the development and implementation of Personalized Medicine approaches.
"*Personalised*" or "*Precision Medicine*" is defined by the Horizon 2020 Advisory group as: "*the medical model using characterization of individuals' phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention*".

Since 2013, the *omics* has assumed a primary role in Personalized Medicine, thanks to its intrinsic characteristic of generating a large amount of data that can be translated into specific profiles of individuals. This leads to the possibility to provide a solid base to transform basic research studies in clinical research ones and beyond.
For this reason, FRRB has decided to invest in promoting and funding multidisciplinary research projects built on partnerships among experts from different areas, with the aim to generate scientific evidence to improve prevention, diagnosis and treatment of diseases, including rare diseases, with a positive impact on the regional health system.
In accordance with the guidelines established by the international Consortium ICPerMed (www.icpermed.eu), FRRB will fund *omics* projects, which might have a more basic approach, as well as projects on *advanced therapies* or *nanotechnologies*, which might have a more clinical approach, with a common goal to improve and implement the Lombardy health system.
In this regard, the projects must necessarily develop one of the following three thematic areas:

- Genomics (and, more generally, studies of "*omics*"), applied to both prospective and retrospective clinical trials;
- Clinical studies based on innovative approaches with advanced therapies, which will contribute to the development of the Lombardy Cell Factory system;
- Development of nanotechnologies and nanomedicines applied to clinical research for better efficiency and therapeutic adherence.

In order for Personalized Medicine to become a common practice, it is necessary to identify tools that can demonstrate the clinical validity of the treatments discovered, as well as the transferability of their results to the Regional Health System, taking into account ethical, social and health implications of personalized treatments.
For this reason, FRRB will promote projects that clearly demonstrate the possibility of using the know-how acquired for the development of new therapies to be used on humans.
In case of basic research projects, the goodness of the idea should be demonstrated through preclinical models.

Thematic area 1: Genomics (and, more generally, "*omics*" studies), applied to both prospective and retrospective clinical trials.

Since the sequence of the human genome has been made available, numerous genomics studies have allowed technological progresses in various fields of research (forensic, animal, environmental sciences, etc.), including biomedical research. Nevertheless, it is still difficult to obtain the association of biological profiles of different individual information with one or more pathologies, with the consequent possibility of developing more targeted and personalized therapies.
The collaborative projects funded under this thematic area will have to develop the analysis of *omics* (genomics, transcriptomics, epigenomics, proteomics, metabolomics, lipidomics, etc.), with the aim of integrating different levels of information deriving from the large quantity of data generated by the *omics,* filling the gap of biological profiles association.
The analysis of the *omics* may be "*prospective*" (cohort studies in which groups of subjects exposed to one or more risk factors are followed over time to evaluate the incidence of a pathology), or "*retrospective*" (case-control studies, whose purpose is to confirm the association of one or more factors with the onset of a disease).
The *omics* topic will have to be developed according to one or more of the following guidelines:

- Identification of subclasses of patients within a given pathology;
- Development of technologies and IT platforms for the analysis and subsequent validation of the huge amount of data generated by the new *omics* technologies;
- Integration of data from different *omics* in order to guarantee a better and more complete characterization of the biological phenomenon under investigation.

If the study will foresee the development of a public database containing data of interest to the scientific community to be used as a reference for subsequent studies, the link to this database, once available, should be published on FRRB institutional website.

Thematic area 2: Clinical studies based on innovative approaches with advanced therapies, which contribute to the development of the Lombardy Cell Factory system

Cell Factories originate from a European interest on the regulation and the development of advanced therapies with the use of cells.
While a drug is a chemical compound that keeps always the same features, a cell is instead a complex entity that can change and adapt to each individual. Although Lombardy is the region that counts the majority of Cell Factories authorized by AIFA (the Italian Medicines Agency), it is still very important to connect the Cell Factory system with researchers interested in studying the therapeutic properties of stem cells and other more differentiated cells potentially useful for their studies.

To this aim, collaborative projects belonging to this area should focus on the use of innovative approaches and ATMPs (Advanced Therapy Medicinal Products), as defined in the "*Reflection paper on the classification of advanced therapeutic medicinal products*", elaborated by the Committee for Advanced Therapies of the "EMA" (European Medicines Agency) in May 2015, allowing the development of new and promising advanced therapies.
Projects related to this area will have to focus on one or more of the following guidelines:

- Genetic therapies that use ATMPs consisting of- or containing recombinant nucleic acids that have the purpose of modifying (repairing, replacing, regulating) a gene sequence, or whose effect is directly related to the sequence of nucleic acids they contain;
- Therapies that use ATMPs consisting of- or containing cells and/or tissues that have been substantially manipulated[1] in order to alter their original characteristics making them more suitable for the clinical use that they want to do or that are not used in the same way in the donor and in the receiver;
- Therapies that use ATMPs that are administered to human subjects for the purpose of diagnosing, treating or preventing a disease;
- Therapies that use engineered tissues to repair or replace human tissue.

Thematic area 3: Development of nanotechnologies and nanopharmaceuticals applied to clinical research for better efficiency and therapeutic adherence

The nanomedicine sector is constantly increasing; currently there are numerous nanopharmaceuticals already on the market and more than 200 are being tested. In fact, nanopharmaceuticals and nanotechnologies have a great therapeutic potential, because they are able, by exploiting their small size (nano-), to transport drug molecules into target tissues, where the drug is released in a targeted and specific manner. Despite this, there are still many target tissues that are difficult to reach with "*classic*" methods and several still inefficient drugs.
The aim of these projects is, therefore, to create new drugs with a particular delivery system that improves their efficacy and safety, as well as the technical characteristics, such as pharmacokinetics and the possibility of reaching target tissues that are difficult to achieve with the currently available systems, with a clear impact on the Lombardy Health System. These projects may involve all therapeutic classes of drugs for which it is possible to develop a drug delivery system.
Projects related to this area will have to follow one or more of the following guidelines:

- Development of nanopharmaceuticals and nanotechnologies that allow the application to clinical practice of the biochemical and cellular information of the molecule under investigation;
- Integration of data from basic research into clinical practice, in particular studies that, once validated in animal models, provide for the possibility of phase I studies;
- Projects that study the possibility of modulating the action of new generation nanostructured drugs in pathological situations in which current therapies are inefficient.

[1] The manipulations described in Annex 1 (http://ec.europa.eu/health/files/eudralex/vol-1/reg_2007_1394/reg_2007_1394_en.pdf) are not considered "substantial".

As previously defined, the research projects financed by FRRB will have to be placed in a context of Personalized Medicine, for which public involvement plays a key role. Therefore, the project proposals must include a communication plan addressed to the scientific community, but above all to the lay public, as FRRB strongly wants to raise awareness on this issue.
The participants to this Call for proposals will have to draft a "*Communication Plan*" for the dissemination of research results, in scientific events (workshops, congresses, etc.) and open events addressed to a non-specialized public (open days with the involvement of patient associations, charity days, brochures, press releases, etc.).
This plan will be analysed by FRRB, which will be interested in being involved in the project events, especially those dedicated to the lay public.
The research projects should also contain an explanation of how they will be aligned with the six fundamental principles of Responsible Research and Innovation (RRI) established by the European Community: governance, public engagement, open access, gender, ethics and science education.
Among these principles, FRRB pays particular attention to gender aspects, and asks the members of the Partnership to indicate their gender policies, by uploading in section "*IX: Attachments*" the "*Gender Equality Plan*" (if existing) and by uploading the form "*Gender Issues Survey*", duly filled, available at the "*IV: Research team*" section.

FRRB is a funding agency that promotes and encourages the participation of female researchers in projects proposals.

TECHNICAL FEATURES

- The eligible organisations, which can apply to the Call, must belong to one of the following categories:
  - Private or public I.R.C.C.S. (Italian Scientific Institutes for Health Research and Health Care)
  - Public Health care providers (ASST)
  - Research Institutes
  - Universities
- The Call is addressed to network of 3 to 5 organisations belonging to one of the categories listed above, which must be located in Lombardy. The Coordinator of the partnership MUST be a IRCCS (private or public) or a ASST.
  A maximum of 2 entities located outside Lombardy or Italy can join in the partnership but will be considered not eligible for funding. They will need to provide a declaration of their interest in participating with their own funds by uploading a document drafted according to FRRB model in the Section "*V: Partners with own fundings*".
- The project budget will amount from a minimum of € 3.000.000 to a maximum of € 5.000.000.
- The project must be innovative, and have characteristics of transferability to the Public Health System.
- The project duration is **36 months**.
- Total budget of the Call: **€ 17.850.000.**

PROJECT EVALUATION

Administrative and technical requirements

FRRB will firstly perform an eligibility check (from an administrative and technical point of view) on all the received proposals. Moreover, FRRB will verify the coherence to the scope of the Call of all the received projects.

Eligible costs

According to the Call text the eligible direct costs are:

- Personnel costs
- Travel costs
- Materials and supplies
- Equipment (on hire or eligible amortisation rate)
- Subcontracting
- Other direct costs

FRRB allows a flat rate of indirect costs calculated as 20% of all the direct costs (subcontracting excluded).

For more information on the budget cost categories and the admitted percentages please read the document "*Guidelines for submission*" published on FRRB institutional web site (www.frrb.it), Section "*Bandi per il finanziamento di progetti di ricerca/Bandi aperti*".

Scientific Revision

Projects, which comply with all the requirements, will proceed to the Scientific Evaluation.
The Scientific Evaluation will involve two distinct Boards:

- International experts, defined as "referees", who will perform a scientific evaluation from remote.
- A panel of experts, defined as "Scientific Committee", who will evaluate projects during a plenary session, called Consensus Meeting.

The Scientific Revision is divided in two phases:

Phase 1: Remote revision

Each project will be assigned to three referees, selected according to the following aspects:

- The referee is an expert of the topic described in the project.
- The referee is an expert of the technologies described in the project.
- The referee has a correspondence to the keywords indicated in the project.

Referees will review projects remotely by providing a numerical vote and a comment.
At the end of the first evaluation phase, the 12 projects with the highest score will proceed to the second evaluation phase.
In case of an equal score of the last projects in the list, all the projects with that score will be admitted to the second evaluation phase.

Phase 2: Consensus Meeting

The Scientific Committee will meet in a plenary session to discuss the projects admitted to the second evaluation phase during a Consensus Meeting.
At the end of the session a final ranking list will be provided and the projects will be funded in order of ranking up to the available resources.
The entire evaluation procedure will be completed within 180 days from the deadline for submission of project proposals.

Table 1: Categories and items of the Scientific Evaluation

Category: EXCELLENCE	
Item 1: Clarity and relevance of the objectives illustrated	0-5
Item 2: Soundness of the hypothesis and of the preliminary data, appropriateness and feasibility of the methodology, including ethical aspects.	0-5
Item 3: Quality of the PI and of the research team	0-5
Category: IMPACT	
Item 1: Advancement beyond state-of-the-art	0-5
Item 2: Quality of the proposal in terms of: a) Dissemination and sharing of results to the scientific community b) Dissemination of results to the lay public c) Description of RRI principles	0-5
Category: QUALITY AND EFFICIENCY	
Item 1: Quality and efficiency of the workplan, of the resources allocated to work packages and of the project structure in line with the objectives.	0-5
Item 2: Appropriateness of the technical and management structures	0-5
Item 3: Quality of the research consortium (PI and partners)	0-5
Item 4: Appropriateness of the distribution of objectives to partners, including a feasibility analysis of each work package compared to partner expertise	0-5

PLANNED TIME SCHEDULE

October 1st, 2018	Opening of the Call
December 14th, 2018 – 5 p.m.	Deadline for electronic submission of project proposals
By February 2019	End of administrative and formal eligibility checks
By May 2019	Scientific Peer Review evaluation
By June 14th, 2019	Publication of final ranking and funding decision