Call 'Preclinical Research in rare diseases: translational steps in large animals'

Development of experimental models and evaluation of therapeutic strategies

In the field of rare diseases, understanding the physiopathological mechanisms and moreover the evaluation of innovative therapeutic strategies, rely for a large part on animal models, particularly rodents. Translational research represents a link between exploratory steps of proofs of principle to clinical application in human. In some cases, the use of larger animal models is necessary to confirm the relevance of a concept or to demonstrate the feasibility, the efficiency and the safety of a therapeutic approach in conditions that mimic as closely as possible the human situation. The call for proposals launched by the French Foundation for rare diseases aims to directly support intermediary key steps towards clinical development for patients.

A – Objectives and major issues of the call for proposals

Eligible: Validation of a proof of concept from *in vivo* model.
Not eligible: Toxicology study.

The objective of this call is to support pilot scientific projects at the interface between the *in vivo* proofs of principle, usually in rodents, and the development of a clinical application in human patients, aiming to improve human well being.

Major issues:
- The project must rely on **scientifically validated preliminary data**,
- The project should in **no way substitute research steps in small animal models** (rodents in particular),
- The **use of a large animal** at this early stage of clinical application **must be justified in terms of specific need and relevance to human pathology** in accordance to ethical rules.

Results should provide essential indications for further clinical development: creation of a specific pathological model, relevance for human disease, feasibility, efficiency, safety of a therapeutic approach.

The program will use a limited number of animals and will answer one or several of the following objectives:

- To contribute to a better understanding and knowledge of the disease and / or to provide a model, a predictive marker of severity or evolution;
- To define new clinical, biological or imaging biomarkers;
- To demonstrate the feasibility, the efficiency and the global safety of the administration of a therapeutic product in relevant model of human pathologies or in a large animal (non human primate, dog, pig etc.);

- To perform pilot study of toxicology and biodistribution mandatory for further development;
- To contribute to technological optimization;
- To develop a new and necessary technical know-how.

The clinical application to the reglementary agency (ANSM) may require a larger number of animals and **specific steps (detailed biodistribution, toxicology study, dose-response study) that are not in the scope of this call.**

The experimental protocol should be clearly exposed, particularly regarding the number of animals, technical protocols, the procedure time, elements of follow-up, different endpoints that will be analyzed (clinical, biochemical, histological, biological). A detailed timetable should be provided. Budget should take into account the whole procedure. Experimental structure and conditions must be appropriate and achievable milestones properly defined and scheduled.

The aim of the call is in compliance with the goals set by the International Rare Diseases Research Consortium (IRDiRC) which was launched in April 2011.

B – Conditions of experimentation

Eligible models: Animals in the scope of this call are usually pigs, sheeps, dogs and non-human primates. Other models may be eligible. The applicant is invited to contact the foundation at aap-bio@fondation-maladiesrares.com to check the relevance and eligibility of the proposed animal model.

Access to platforms: Experiments in large animals will be performed in a specific adapted research structure, partner of the French Foundation for rare diseases, that is in agreement with the European regulatory agencies (Directive 2010/63, décret 2013-118). Information can be provided to the project leader concerning adapted centers allowing the technical realization of the research project.

The project will be developed in close interaction between dedicated member(s) of the research team and the platform.

The selection of the platform will be performed according to the relevance and orientation of the project and in order to allow optimization of the handling of projects by the platform, according to its expertise in specific types of models, technical specificity, equipment, capacity and calendar, with the aim to deliver optimal results to the research team.

Project will be submitted for ethical approval before examination by the Ministry of Higher Education and Research for authorization.

Results and Intellectual Property data resulting from projects funded through the call will be owned by the researcher's organizations.

C – Evaluation

C1. Eligibility

The principal investigator of the project must belong to a French research team**,** affiliated to academia (research team working in universities, other higher education institutions or research institutes) and/or to clinical/public health sector (research team working in state or university hospitals/public health organizations).

C2. Evaluation criteria

The following elements will be particularly considered in the evaluation of the project

- Originality of the project;
- Relevance of preclinical results already obtained in small animals;
- Detailed description and time table of the research program proposed;
- Clarity of objectives and outcomes of the project;
- Prospects in terms of therapeutic benefits;
- Quality of the team;
- Integration of the project in the research program of the applicant;
- Complementary and synergy of associated partners on the project;
- Positioning of the project in the national and international context.

C3. Selection

Pre-proposals will be selected by a scientific *ad hoc* committee, composed of large animal models experts and members of the Scientific Advisory Board of the French Foundation for rare diseases. The decision on applications selection and invitation to full proposal will be communicated at the beginning of January 2018.
Full proposals will be evaluated by two external referees, then selected by the scientific *ad hoc* committee.

D – Funding

The French Foundation for rare diseases will provide financial support for a maximal amount of 100 000€.
Funding will cover services costs of the platform that may include purchase, housing and running costs and technician cost for experiments.
Funding is not intended to cover equipment, operating or personnel costs in the researcher's laboratory.

E – Proposal submission and schedule of the call

There will be a **two-stage submission procedure for applications**: pre-proposals and full proposals.

To complete and submit an application form, please access to the portal "**Applicant portal**".

Submission deadline for pre-proposals: **October 24, 2017 (5:00 pm)**.
The provisional schedule of the call is the following:

September, 2017	Launch of the call
October 24, 2017	Submission deadline for pre-proposal
February 08, 2018	Submission deadline for full proposal
March 2018 – April 2018	Evaluation and selection process
May 2018	Notification of results

The title of the selected projects and name of their principal investigator will be published on the website of the French Foundation for rare diseases. The summary written for a general audience may be used for communication purposes by the Foundation.

Acknowledgement Policy: It is required that projects funded by the French Foundation for rare diseases be acknowledged in all publications and communications. Reference(s) of the publication(s) must be sent to the foundation.

IRDiRC policies and guidelines: the project partners are expected to follow IRDiRC policies and guidelines. For more information see http://www.irdirc.org.