FONDATION Maladies Rares

CALL FOR PROPOSALS 2024

- TRANSLATIONAL RESEARCH -

Preclinical Research in rare diseases: translational steps in large animals

Submission deadline for applications: **January 16th, 2025, 5:00 pm (CET)**

CONTEXT AND OBJECTIVES

Translational research works at the interface between basic science and clinical research to promote the translation of scientific discoveries into medical applications for patients. The aim of preclinical research projects is to use physiologically relevant models to demonstrate that potential treatments identified in basic research projects could work in humans.
While basic research uses cells or small animal models such as flies, fish or rodents to understand the pathophysiological mechanisms of disease and identify new therapies, translational research often requires the use of larger animals. Although ongoing technological innovations, such as the development of organoids, are increasingly replacing the use of animal models, in vitro models are unable to faithfully recapitulate complex physiological environments and the use of animal models is still essential for some scientific projects. Indeed, to demonstrate the feasibility, efficacy or safety of a therapeutic proof of concept, an organism with a size, weight or anatomy close to that of humans may be a must. For example, biodistribution and toxicity tests are very limited in in vitro models and even more relevant in large animal models than in rodents.

In this context, the present call launched by the Foundation for Rare Diseases aims to directly support key intermediate steps of preclinical research projects towards clinical development for human patients affected by rare diseases by funding translational steps in large animals, either by developing new disease models or by testing therapeutic proof of concept.

PROGRAM DESCRIPTION

The objective of this call is to support scientific projects at the interface between in vivo proof of concept, usually in rodents, and the development of clinical applications in patients to improve human well-being. The results should provide essential indications for further clinical

development: creation of a specific pathological model, testing the relevance, feasibility, efficacy or safety of a therapeutic approach in human patients.

Projects validating proof of concept from an in vivo model in a large animal are eligible.

Key requirements:

- The project must be based on validated preliminary data,
- The project should in no way replace research in small animal models, particularly rodents,
- At this early stage of clinical application, the use of a large animal must be justified in terms of specific need and relevance to human pathology.

The project should address one or more of the following objectives:

- Contribute to a better understanding of the disease, provide a new model or predictive marker of severity or progression,
- To define new clinical, biological or imaging biomarkers,
- To demonstrate the feasibility, efficacy or safety of the administration of a therapeutic product in a relevant large animal model,
- To perform pilot toxicology and biodistribution studies necessary for the further development of the future therapy,
- To contribute to technological optimisation,
- To develop new and necessary technical know-how.

The programme must use a **limited number of animals**. An application to the National Agency for Medicines (ANSM, www.ansm.sante.fr) may require more animals and other experiments, such as detailed biodistribution, toxicology or dose-response studies, which are outside the scope of this call.

The experimental protocol should be clearly disclosed, particularly with respect to the number of animals, technical protocols, duration of procedures, elements of follow-up, endpoints and samples to be analysed - clinical, biochemical, histological and biological. The experimental design and conditions must be appropriate, and achievable milestones must be properly defined and scheduled.
A detailed schedule and budget should be provided and should cover the entire procedure.

This programme is open to research projects covering all rare diseases.

For rare cancers, the French National Cancer Institute (INCa) and the FFRD have jointly defined the following criteria:

- High throughput sequencing projects concerning primary malignant tumours should be addressed to the INCa,
- Projects concerning benign tumours as well as systemic rare diseases involving tumour development will be evaluated within this call.

In the case of neuromuscular diseases, close consultation with the AFM-Téléthon could determine the most appropriate support in terms of the scope of the call.

SPECIFIC CONDITIONS OF EXPERIMENTATION

Animals covered by this call are normally rabbits, minipigs, pigs, sheep, cats, dogs and non-human primates, but other models may be eligible. The applicant is invited to contact FFRD by email at aap-bio@fondation-maladiesrares.com to check the eligibility of other animal models.

Experiments on large animals must be performed in adapted research structures in accordance with the European regulatory authorities (Directive 2010/63 and Directive déléguée 2024/1262). Thus, experiments will be performed by a specific technological platform and the project will require close interaction between the applicant's research team and the dedicated platform.

The selection of the platform should be based on:

- Relevance to the project in order to optimise the handling of the project by the platform,
- Expertise of the platform in specific animal models,
- Availability of specific techniques/equipment required for the project on the platform and,
- Capacity of the platform to carry out the project within the time schedule.

If the project is selected for funding, it should be submitted for ethical approval to the Ministry of Higher Education and Research. Funds will not be released until ethical approval has been received.

ELIGIBILITY

The Principal Investigator of the study must be part of a French research team affiliated to the academic sector (research team working in universities, other higher education institutions or research institutes) and/or the clinical/public health sector (research team working in hospitals/public health organisations).

Early career researchers are encouraged to apply as Principal Investigators.

EVALUATION

Pre-proposals will be selected by a dedicated Scientific Committee composed of members of the FFRD Scientific Advisory Board and experts in the field, based on the following criteria:

- Scientific quality and ambition
- Project organisation and implementation

Full proposals will be peer-reviewed by at least two national or international academic experts in the field and selected by a dedicated Scientific Committee composed of members of the FFRD Scientific Advisory Board and experts in the field, based on the following criteria:

- Relevance and significance of the project,
- Project quality and scientific soundness,
- Feasibility of the project,
- Innovation,
- Quality of the applicant and quality of the laboratory.

FUNDING

FFRD will provide financial support up to a maximum of 100 k€ per project.

Funding will cover the costs of the platform, which may include purchase, housing, running costs and technician costs for experiments.

It is not intended to cover the costs of the applicant laboratory.

Overheads are not allowed by the FFRD.

SUBMISSION AND SCHEDULE

Applications can only be submitted via the FFRD Synto online platform: https://ffrd.syntosolution.com/ .

Provisional schedule:

Launch of the call	November 2024
Submission deadline for pre-proposals	January 16, 2025, 5:00 pm (CET)
Notification of results for pre-proposals	Mars 2025
Submission deadline for full proposals	April 8, 2025, 5:00 pm (CET)
Notification of final results	July 2025

Results will be communicated by e-mail to the applicant.

Applicants resubmitting projects must provide a detailed response to the comments made by the FFRD Scientific Committee at the previous call, highlighting the changes in the revised version.

Applicants who are part of a research team already funded by the FFRD since 2017 must have provided a detailed report on the results and impact of any completed project(s). For ongoing projects, a progress and/or preliminary data report is required.

Report forms are available in the Applicant Portal ("Documentation" tab) or upon request by e-mail at aap-bio@fondation-maladiesrares.com. Please attach all reports to the proposal in the appropriate section.

FAIR policy / IRDiRC policies and guidelines

By submitting a project to this call, applicants agree to comply with the following requirements: FAIR guiding principles for scientific data management and stewardship.

The objectives of the call are in line with the objectives of the International Rare Diseases Research Consortium (IRDiRC). Applicants are expected to follow IRDiRC policies and guidelines.

COMMUNICATION

Applicants must agree that the title and non-confidential abstract of funded projects, as well as the name and affiliation(s) of the Principal Investigator(s), will be made public and published on the FFRD website: http://fondation-maladiesrares.org.

ACKNOLEDGEMENT POLICY

Applicants must acknowledge the FFRD as the source of funding in all communications related to the project (posters, oral presentations, scientific publications, etc.) using the terms

"Foundation For Rare Diseases" or "Fondation Maladies Rares" and/or the FFRD logo (available upon request). Reference(s) to the publication(s) must be sent to the FFRD by email to aap-bio@fondation-maladiesrares.com

CONTACT

Please contact aap-bio@fondation-maladiesrares.com with any questions relating to this call.