FONDATION Maladies Rares

CALL FOR PROPOSALS 2025

- SCREENING -

Identifying new therapeutic molecules for rare diseases

Submission deadline for applications: **September 4th, 2025, 5:00 pm (CET)**

CONTEXT AND OBJECTIVES

Currently, around 3 million people in France are affected by a rare disease, and approximately 95% of these patients lack any available therapeutic options. This call aims to support scientific research projects focused on identifying new molecules with potential for therapeutic application, with the goal of developing innovative treatments for individuals living with rare diseases.

To achieve this objective, the call will support projects addressing one or more of the following key stages of the drug discovery pipeline:

1. **High-Content/High-Throughput Screening (HCS/HTS)**

HCS or HTS methodologies using chemical libraries to identify biologically active compounds ("hits") with potential therapeutic relevance.

2. ***In vitro* mechanistic screening**

Detailed *in vitro* investigation of specific signalling pathways, to validate and further characterize targeted pathways and potential hits identified through previous broad screening efforts.

3. **Hit-to-Lead optimization**

Refining and optimizing hit compounds to improve their pharmacological properties and drug-like profiles, thereby advancing them toward lead compound status.

PROGRAM DESCRIPTION

Prerequisites:

- The project is supported by robust and validated preliminary data.
- A relevant biological model has been identified and validated either by the proposing research team or in collaboration with a consortium.
- The experimental model faithfully recapitulates a physiologically relevant pathway involved in the disease mechanism, with well-defined and quantifiable readouts.
- The proposal clearly demonstrates the relevance and rationale of the screening assay for identifying compounds capable of reversing the disease pathophysiology.

1. High-Content/High-Throughput Screening:

The project should focus on the development of a **miniaturized, automated, robust, and reproducible assay**, serving as a critical entry point for the identification and selection of hit compounds with potential for downstream drug development. Clear, quantifiable, and

biologically relevant readouts must be established and validated **prior to proposal submission**.

The project may comprise two core components:

- Miniaturization of an existing biological model already established in the applicant's laboratory.
- Automation of this model to enable its application in HTS/HCS campaigns.

To ensure the assay is suitable for scalable screening, the proposal must describe key optimization parameters, including:

- **Type of assay:** Specify whether the assay is target-based or process-based; and indicate whether it is biochemical or cell-based. For cell-based assays, detail the use of relevant biological systems (e.g., primary cells, established cell lines, or iPSC-derived models) along with disease-specific and appropriate control conditions. Where feasible, discuss plans for validation in whole-organism models.
- **Detection technology:** Describe the signal detection method (e.g., luminescence, fluorescence, absorbance), and its compatibility with the selected assay format.
- **Reagents:** Provide a list of essential reagents such as cell lines, antibodies, recombinant proteins, enzyme substrates, or other assay-specific components.
- **Readout adaptation:** Indicate any modifications made to optimize readout conditions (e.g., signal intensity, dynamic range, background reduction).
- **Instrumentation:** Specify the equipment required for assay implementation, including any specialized platforms for automation or high-throughput analysis.

2. *In vitro* mechanistic screening

The project should focus on elucidating the molecular mechanisms underlying the mode of action of a potential therapeutic *in vitro*, with the goal of deepening the understanding of specific signalling pathways and refining the functional role of hits previously identified through large-scale screening approaches. Mechanism-based screening strategies must be employed to guide the identification and development of next-generation therapeutic candidates.
Proposals must centre on a defined subset of signalling pathways and articulate a clear, hypothesis-driven experimental framework.
Relevant research areas include, but are not limited to: intracellular signalling cascades, gene regulatory networks, protein interaction dynamics, and cellular behaviour. All studies must be performed *in vitro* using well-justified and biologically relevant cellular model systems.

3. Hit to Lead optimization

The project must build on promising hits previously identified during an earlier screening campaign.

The optimization of these identified hits involves two main phases:

- **Hits confirmation and profiling:** Validate and prioritize a focused set of molecules using complementary approaches by ranking and clustering hits. It includes confirmatory assays, dose-response studies, orthogonal and biophysical testing, and secondary screens, synthesis pathways, *in silico* profiling, etc.

- **Lead discovery:** Assess the optimization potential of confirmed hits to identify the most promising compounds. Selected candidates undergo limited optimization to achieve proof of concept in animal models, integrating both experimental and computational strategies.
  Projects in the lead discovery phase may include:
    - Validation of hits or candidate drugs (whether from screening or literature) in relevant disease models,
    - Assessment of pharmacological activity, physicochemical properties, ADME-Tox profiles, and pharmacokinetics (PK),
    - Testing of a small set (minimum three) of analogues to establish quantitative structure-activity relationships (QSAR),
    - Optimization of compound properties such as target affinity, metabolic stability, and selectivity.

This program is open to research projects focused on all rare diseases.

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

- Projects focused on primary malignant tumors should be submitted to INCa,
- Projects addressing benign tumors or systemic rare diseases with tumor development will be considered within this call.

Each research team is eligible for funding of only one project under this call.

INVOLVEMENT OF TECHNOLOGICAL PLATFORMS

FFRD has formed partnerships with several technological platforms, offering a wide range of expertise, skills, and services.

Collaboration with a partner platform is required for HTS/HCS projects. However, in vitro mechanistic screenings and hit-to-lead campaigns can either be conducted in the applicant's own laboratory or in collaboration with a platform.

Principal investigators are encouraged to contact FFRD partner platforms for detailed information on available services and associated costs that align with their project objectives, and to receive support in optimizing the technical design.

A list of partnering platforms can be found on the FFRD website: https://fondation-maladiesrares.org/en/plateformes-partenariats/.

If specific needs are not addressed by the partnering platforms, please reach out to FFRD at aap-bio@fondation-maladiesrares.com to discuss the eligibility of alternative platforms and service conditions.

ELIGIBILITY

1. Projects

To be considered eligible, proposals must align with the objectives of the call and meet all criteria outlined in the 'Program Description' section, including full compliance with the prerequisites specified above.
HTS/HCS proposals must include a quotation from the relevant technology platform; submissions lacking this documentation will be deemed ineligible.
Projects involving the use of animal models are strictly excluded from this call.
Any proposal that fails to fully adhere to the requirements detailed in the online submission form will be deemed ineligible without exception.
To be eligible, projects must last between 12 and 24 months.

2. Principal Investigator

The principal investigator of the study must be part of a French research team, affiliated with academia (such as universities, higher education institutions, or research institutes) and/or the clinical/public health sector (including hospitals or public health organizations).
Early-career scientists are strongly encouraged to apply as principal investigators.

FUNDING

For HTS/HCS projects, funding will cover only the costs associated with the technological platform (services and consumables). A quote from the technological platform must be submitted along with the application.

For *in vitro* mechanistic screenings and hit-to-lead campaigns, funding will cover only services and consumables. Equipment and personnel costs within the applicant's laboratory are not covered by this funding.

FFRD will provide financial support of up to a maximum of €40,000 per project.
Co-financing of the project is allowed; however, the same item of expenditure cannot be funded by multiple sources.

Overhead costs are not eligible for FFRD funding. Additionally, FFRD grants are exempt from VAT.

SUBMISSION AND SCHEDULE

Applications must be submitted exclusively through the FFRD Synto online platform : https://ffrd.syntosolution.com/. Applications sent by e-mail or by any other means will not be considered. The application form and the documents to be provided are detailed on the online portal.

The candidate and their director must have created and completed their profiles on the Synto platform before submitting the project. Please consult the tutorials available in the 'Documentation' section of the Synto platform for guidance.
Technical support is available from the launch of the call until 24 hours before the submission deadline. Candidates are responsible for anticipating any potential issues in a timely manner, as no extensions will be granted after the call for proposals has closed.

Provisional schedule:

Launch of the call	June 10, 2025
Submission deadline for application	September 4, 2025 - 5:00 pm (CET)
Notification of the results	December 2025

Applicants resubmitting projects must provide a detailed response to the comments from the FFRD scientific committee from the previous session and clearly highlight the changes made in the revised version.

Applicants from research teams that have received FFRD funding since 2017 must submit a detailed report for all completed projects if this report has not already been submitted to the FFRD. For ongoing projects, a progress report and/or preliminary data must be provided. Report forms are available on the applicant portal (tab 'Documentation') or upon request by e-mail at aap-bio@fondation-maladiesrares.com. Please attach all reports to the proposal in the appropriate section.

EVALUATION

Applications will be evaluated by a minimum of two national or international academic experts in the relevant field and selected by a dedicated scientific committee. This committee will include members of the FFRD Scientific Advisory Board and field experts, and selections will be 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.

Results will be sent directly via email through the FFRD Synto online platform. Please ensure that emails from "FFRD by Synto" are not filtered into your spam folder.

ADMINISTRATIVE AND FINANCIAL MONITORING

A research agreement will be signed between the managing institution of the selected applicants and the FFRD. This agreement will outline the scientific and financial monitoring requirements for the project. It will come into effect only after approval by the relevant ethical bodies, where applicable.

Successful applicants commit to submitting project monitoring reports as requested by the FFRD, using the templates provided, and to reporting on project progress upon request.

FAIR POLICY / IRDiRC POLICIES AND GUIDELINES

By submitting a project to this call, applicants agree to adhere to the FAIR guiding principles for scientific data management and stewardship.
The objectives of this call align with the goals set by 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, along with the principal investigator's name and affiliation(s), will be published on the FFRD website: https://fondation-maladiesrares.org/projets-de-recherche-laureats/.

ACKNOLEDGEMENT POLICY

Applicants must acknowledge the FFRD as a funding source in all project-related communications (posters, oral presentations, scientific publications, etc.) by using the terms “Foundation For Rare Diseases” or “Fondation Maladies Rares” and/or by including the appropriate logo (available upon request).
Reference(s) of the publication(s) must be sent to the FFRD via e-mail to aap-bio@fondation-maladiesrares.com.

CONTACT

For any questions related to this call, please contact aap-bio@fondation-maladiesrares.com.