E-Rare-3 Call for Proposals 2016 for
"Clinical research for new therapeutic uses of already existing molecules (repurposing) in rare diseases"

Preliminary Announcement

The ERA-Net “E-Rare” for research programmes on rare diseases has been extended to a third phase “E-Rare-3” (2014-2019) to further help in coordinating the research efforts of European countries in the field of rare diseases and implement the objectives of International Rare Disease Research Consortium (IRDiRC).

The following parties,

- Austrian Research Promotion Agency (FFG), Austria
- Canadian Institutes of Health Research (CIHR), Canada
- Fonds de recherche du Québec (FRQS), Canada, Québec
- French National Research Agency (ANR), France
- Direction Générale de l'Offre de Soins (DGOS), France
- German Federal Ministry of Education and Research (BMBF), Germany
- German Research Foundation (DFG), Germany
- National Research, Development and Innovation Office (NKFIH), Hungary
- Chief Scientist Office of the Ministry of Health (CSO-MOH), Israel
- Italian Ministry of Health (MoH), Italy
- State Education Development Agency (Valsts izglītības attīstības aģentūra VIAA), Latvia
- Narodowe Centrum Badań i Rozwoju (NCBR), Poland
- Foundation for Science and Technology (FCT), Portugal
- Executive Agency for Higher Education, Research, Development and Innovation Funding (UEFISCDI), Romania
- National Institute of Health Carlos III (ISCIII), Spain
- Swiss National Science Foundation (SNSF), Switzerland
- The Scientific and Technological Research Council of Turkey (TUBITAK), Turkey

intend to open the eighth E-Rare joint call for funding multilateral research projects on rare diseases. The call is expected to be opened simultaneously by the parties in their respective countries.

Please note that decision about the participation of the funding agencies is still pending. The final list of participating funding agencies will be published in the Call text.
1. AIM OF THE CALL

The aim of the call is to enable scientists in different countries to build an effective collaboration on a common interdisciplinary research project based on complementarities and sharing of expertise, with a clear translational research approach. Projects shall involve a group of rare diseases or a single rare disease following the European definition i.e. a disease affecting not more than five in 10,000 persons in the European Community, EC associated states and Canada.

TOPICS OF THE CALL

The specific objective of this call is to promote the clinical and pre-clinical proof of concept studies for the potential application of medicinal products that are either already marketed or having achieved a significant stage in the development process in rare indications. Projects should aim at discovering new therapeutic uses for Agents whose clinical safety has already been documented to move quickly into proof of concept trials in the selected rare diseases’ patient population.

Registered medicinal products or Agents that have been shown to be safe, but have failed to meet end points of their originally-targeted indications in late-stage trials, can leverage their inherently reduced development risks into potentially new indications. Since safety accounts for approximately 30% of drug failures in clinical trials, this is a significant development advantage that so-called repositioned products enjoy. When such products enter into clinical trials, they compete with non-repositioned products not in terms of safety, but in terms of efficacy and significant benefit against standards of care in the new indications investigated.

Two types of projects are eligible for this call:

- Type A: Preclinical studies to verify target engagement and to perform additional toxicity testing if necessary (for example in the case of paediatric indications where juvenile animal studies might be warranted) in a disease model for a maximum period of one year followed by the implementation of Phase 1b or Phase 2a clinical trials at the beginning of the second year of the project. For this call, Phase 1b, and Phase 2a trials are defined as follows: Phase 1b trials are defined as studies usually conducted in the target patient population to establish feasibility (e.g., target engagement, pharmacodynamics/pharmacokinetics (PD/PK), initial dosing of the Agent) prior to a Phase 2a trial. Phase 2a clinical trials provide data on the relationship of dosing and response for the particular intended use (including trials on the impact of dose ranging on safety, biomarkers, and proof of concept), typically 150 subjects or less for trials in adults.

- Type B: Milestone-driven Phase 2 clinical trials to demonstrate that the Agent modulates the target and has the potential to yield the desired clinical outcome in the proposed disease population for a period up to three years.

Proof of concept trials can include, as examples:

- Use of the Agent(s) as stand-alone interventions,
- Use of the Agent(s) as adjunctive interventions (if there is no evidence of drug-drug interactions with the proposed standard of care treatment).

It is mandatory that there is reliable existing data for the Agents safety profile (e.g. approved for other therapeutic indication, off-label use or well established use, development up to Phase 2 for other indication has been successful).
Please note that for the success of the project, most of the following criteria shall be fulfilled:

- Existing knowledge of natural history of the rare indication(s)
- Existence of a quality patient registry or database
- Existence of an unmet medical need
- Definition of strategies to inform the selection of patients for proposed new uses of the Agent(s) should be specified.

Please note the following recommendations:

- It is recommended that projects focused on clinical trials (type B) have already started the process in order to obtain a Scientific Advice / Protocol Assistance from EMA (http://www.ema.europa.eu/ema/), and if relevant, have already applied for an orphan designation (in accordance with IRDiRC Recommendations, (REF)). However, please note that eligibility of fees applied by EMA for the protocol assistance is depending on national rules.
- The innovative therapeutic approaches with potential use in cluster of several diseases will be considered of high added value.
- Projects shall engage patient representatives all along the study, in particular in the design of the studies and the selection of endpoints.
- Projects shall have identified a corporate partner to take the product to marketing authorisation, or make it an objective in the course of the project.

The research projects submitted within this call must be based on novel ideas stemming from consolidated previous results and must be clearly endowed with a strong translational research orientation, i.e. bench to bed studies allowing a rapid implementation into public health-related decisions or into the clinics. In order to achieve this goal, the necessary expertise and resources should be brought together from academia, clinical/public health sector and private companies. The research teams within a consortium should include investigators from all scientific disciplines, research areas and expertise necessary to achieve the proposed objectives.

The research proposals must demonstrate complementary and synergistic interaction among the partner teams. There should be clear added value in the transnational collaboration over the individual projects, in term of:

i) Gathering a critical mass of subjects/patients and or subjects/patients databases and corresponding biological materials that would not be possible at a national scale;

ii) Sharing of resources (biobanks, models, databases, diagnostic tools, etc.) of specific know-how and/or innovative technologies, and of expertise. The projects should address the issues of potential efficacy and cost-effectiveness of the proposed interventions and also clearly demonstrate the potential health impact.

The use of existing European health research infrastructures is strongly encouraged when appropriate, e.g. research infrastructures established as an European Research Infrastructure Consortium (ERIC) or identified on the roadmap of the European Strategy Forum on Research Infrastructures (ESFRI). Projects are invited to identify the existing European research data infrastructures that may be used and how these may be mobilised,
in particular for long-term data curation and preservation (in accordance with EU and IRDiRC recommendations, REF).

The following ESFRI European Research Infrastructures were identified as potentially useful for this kind of study:

- Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) - http://bbMRI-ERIC.eu/about
- European Advanced Translational Infrastructure in Medicine (EATRIS) - http://www.eatris.eu/
- The European Clinical Research Infrastructures Network (ECRIN) - http://www.ecrin.org/
- The European Life Sciences Infrastructure for Biological Information (ELIXIR) - http://www.elixir-europe.org/
- European Infrastructure of Open Screening Platform for Chemical Biology (EU-OPENSCREEN) - http://www.eu-openscreen.eu/
- European Infrastructure for Phenotyping, Archiving and Distribution of Mouse Models (INFRAFRONTIER) - https://www.infrafrontier.eu/

The following approaches and topics are excluded from the scope of the call:

- Development of new models of diseases
- Discovery and early development of new compounds
- Feasibility studies of devices
- Preliminary studies of radiation, surgical, behavioural or rehabilitation therapies
- Studies on advanced therapies (gene therapy, cell therapy)
- Clinical studies concerning rare infectious diseases, rare cancers and rare adverse drug events or secondary outcomes in treatments of common diseases
- Compassionate use

2. GENERAL CONDITIONS FOR APPLICATION

Joint research proposals may be submitted by higher education institutions, non-university public research establishments, hospitals as well as commercial companies, in particular small and medium-size enterprises (SMEs), according to relevant national funding organisations’ regulations for research funding.

Only transnational projects will be funded. Each consortium submitting a proposal must involve a minimum of three eligible and a maximum of six eligible partners from at least three different countries participating to the call (see list above). Not more than two eligible partners from the same country participating in the call will be accepted in one consortium. In order to recruit the necessary patient numbers for the proposed study, a consortium may need to collaborate with other centres. If the unique role of those centres is providing patients data and/or samples for the study only, they will not be considered as partners of the consortium but can be included otherwise, e.g. via cooperation agreements or subcontracting.

Applicants are encouraged to include partners from the participating Eastern European countries (Hungary, Latvia, Poland, Romania and Turkey). If they include such partners, the maximum number of eligible partners can be increased to eight (see table below).

Additional partners that secure their own funding may join consortia. However, their number is limited to two. The consortium coordinator must always be eligible to receive
funding from the funding organisations participating in the call. Only groups that contribute substantially to at least one of the work packages are considered as partners. They must state clearly in the proposal if these funds are already secured or if not, how they plan to obtain funding in advance of the project start. It will be required to document the availability of their funds before October 1, 2016.

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<tr>
<th>Number of partners requesting funding</th>
<th>Possible number of additional partners with own funding</th>
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<td>7 (only possible with inclusion of 1 Eastern European partner)</td>
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<td>8 (only possible with inclusion of 2 Eastern European partners)</td>
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Whilst applications will be submitted jointly by groups from several countries, individual groups will be funded by the individual E-Rare-3 funding organisation respective of the country from which applicants have applied. The applications are therefore subjected to eligibility criteria of individual funding organisations.

Applicants are strongly advised to contact their national representative and confirm eligibility with their respective funding organisations in advance of submitting an application.

3. TIMETABLE

There will be a pre-registration procedure followed by a two-stage submission/evaluation procedure for joint applications. The call is scheduled to open on 7th of December, 2015. The indicative deadline for pre-registration is February 1, 2016. The indicative deadline for submitting the full proposals is March 3, 2016. An independent international Scientific Evaluation Committee will carry out a scientific evaluation according to specific evaluation criteria. Based on this central evaluation, selected consortia will be invited to submit joint rebuttal / modified proposals by July 18, 2016.

For further information, please visit us on the website: http://www.e-rare.eu

For questions regarding the joint call please contact the Joint Call Secretariat:

E-RareCalls@agencerecherche.fr
Dr. Juliane Halftermeyer [+33 1 78098022]

For questions regarding national eligibility criteria and requirements please contact the national contact persons listed below.
Please Note:

The information provided in this pre-announcement is indicative, may be subject to changes and is not legally binding to the funding organisations.

Additional funding organisations might join the call before the official publication.

Interested applicants are encouraged to initiate scientific contacts with potential project consortium partners for applications.
# National/regional contact details

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<tr>
<th>Country/Region</th>
<th>Institution</th>
<th>Website</th>
<th>National/regional contact</th>
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<tr>
<td>Austria</td>
<td>FFG</td>
<td><a href="https://www.ffg.at/seka">https://www.ffg.at/seka</a></td>
<td>Corinna.wilken [+43 (0)5 7755 – 1317] <a href="mailto:Corinna.wilken@ffg.at">Corinna.wilken@ffg.at</a></td>
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<td>Canada, Québec</td>
<td>FRQS</td>
<td><a href="http://www.frqs.gouv.qc.ca">www.frqs.gouv.qc.ca</a></td>
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<td>France</td>
<td>ANR</td>
<td><a href="http://www.agence-nationale-recherche.fr/">www.agence-nationale-recherche.fr/</a></td>
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<td>France</td>
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<td><a href="http://www.sante.gouv.fr/la-direction-generale-de-l-offre-de-soins.html">www.sante.gouv.fr/la-direction-generale-de-l-offre-de-soins.html</a></td>
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<td>Germany</td>
<td>BMBF</td>
<td><a href="http://www.gesundheitsforschung-bmbf.de">http://www.gesundheitsforschung-bmbf.de</a></td>
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<td>Latvia</td>
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<td>Country</td>
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<td>Portugal</td>
<td>FCT</td>
<td><a href="http://www.fct.pt">www.fct.pt</a></td>
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<td>Romania</td>
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