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

Pre-registration deadline for projects: February 1, 2016

Submission deadline for proposals: March 3, 2016

The links to proposal template, electronic proposal submission, guidelines for applicants and further information can be found at the E-Rare website

www.e-rare.eu

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Call text

1. MOTIVATION

There are at least 6000 to 7000 distinct rare diseases, the great majority being of genetic origin. Although individually rare, taken together rare diseases affect at least 26-30 million people in Europe. Moreover, they represent a major issue in health care: a large number of these diseases lead to a significant decrease of life expectancy and most of them cause chronic illnesses with a large impact on quality of life and the health care system.

Therefore, research on rare diseases is needed to provide knowledge for prevention, diagnosis and better care of patients. Yet, research is hampered by lack of resources at several levels: (1) Few scientists work on one specific disease, (2) There are few patients per disease and they are scattered over a large geographic area, causing difficulties to gather the necessary cohorts, (3) Existing databases and material collections are usually local, small, and not accessible or standardised, (4) Diseases often have complex clinical phenotypes and require interdisciplinary cooperation for research, hence, interdisciplinary approaches to treatment.

The specificities of rare diseases - limited number of patients, scarcity of relevant knowledge and expertise, and fragmentation of research - single them out as a distinctive domain of very high European added-value. Rare diseases are therefore a prime example of a research area that can strongly benefit from collaboration/coordination on a transnational scale.

In this context, 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[1]).
The following parties,

- Austrian Research Promotion Agency (FFG), Austria
- Fonds zur Förderung der Wissenschaftlichen Forschung (FWF), Austria
- Research Foundation – Flanders (FWO), Belgium (Flanders)
- Canadian Institutes of Health Research (CIHR), Canada
- Fonds de recherche du Québec - Santé (FRQS), Canada, Québec
- French National Research Agency (ANR), France
- Ministère des Affaires sociales, de la Santé et des Droits des femmes (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
- National Institute of Health Carlos III (ISCIII), Spain
- Swiss National Science Foundation (SNSF), Switzerland
- The Scientific and Technological Research Council of Turkey (TUBITAK), Turkey

[1] http://www.irdirc.org

have decided to open the eighth E-Rare joint transnational call (JTC 2016) for funding multilateral clinical research projects on rare diseases. The call is being opened simultaneously by the parties in their respective countries. In addition, Patient Organisations (PO) - represented in this call mostly by EURORDIS - may also co-fund selected projects based on their mandate and research topic interest (see section 6.2 for details).

2. AIM OF THE CALL

The aim of the E-Rare Joint Transnational Calls (JTCs) 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.

The specific objective of this call is to promote 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.

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.

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).
- 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,

or

- 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, www.irdirc.org). 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 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, www.irdirc.org).

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

- The European Clinical Research Infrastructures Network (ECRIN) - http://www.ecrin.org/
- European Advanced Translational Infrastructure in Medicine (EATRIS) - http://www.eatris.eu/
- Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) - http://bbmri-eric.eu/about
- European Infrastructure for Phenotyping, Archiving and Distribution of Mouse Models (INFRAFRONTIER) - https://www.infrafrontier.eu/
- 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

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

3. MANAGEMENT BOARDS

Two boards, the Call Steering Committee (**CSC**) and the Scientific Evaluation Committee (**SEC**), will manage the evaluation process of the call with support of the Joint Call Secretariat (**JCS**) (set up at ANR, France). SEC and CSC members will not submit or participate in proposals within this call. The process includes a 2 stage submission/evaluation procedure, including the final selection and award of research projects.

- **The Call Steering Committee (CSC)** is composed of a single representative from each country/region funding organisation and a representative of the patient organisation alliance EURORDIS. The CSC will supervise the progress of the call and the evaluation of proposals. The CSC will make the final funding recommendation to the national/regional funding organisations and to patient organisations interested in

co-funding a specific project in their area of interest on the proposals to be funded, based on the final ranking list provided by the SEC. All decisions concerning the call procedures will be taken by the CSC.

- **The Scientific Evaluation Committee (SEC)** is a panel of internationally recognised scientific experts responsible for the evaluation of submitted proposals. SEC members must sign a confidentiality form and a statement to confirm that they do not have any conflicts of interest.

4. APPLICATION

4.1. Funding recipients/Eligibility

Joint research proposals may be submitted by applicants belonging to one of the following categories (according to country/regional regulations):

- academia (research teams working in universities, other higher education institutions or research institutes)
- clinical/public health sector (research teams working in hospitals/public health and/or other health care settings and health organisations)
- enterprise (all sizes of private companies). Participation of small and medium-size enterprises (SMEs) is encouraged when allowed by national/regional regulations.

➢ Please note that the inclusion of a non-eligible partner in a proposal **leads to the rejection of the entire proposal without further review**. Whilst applications will be submitted jointly by research partners from several countries, individual groups will be funded by the individual funding organisation of their country/region that is participating in the E-Rare-3 JTC 2016. The applications are therefore subjected to **eligibility criteria of individual funding organisations**. Applicants are strongly advised to contact their corresponding national/regional representative and confirm eligibility with their respective funding organisations in advance of submitting an application (see national/regional contact details and Annex). **The adherence to the national/regional regulations in the "Guidelines for applicants" document is mandatory.**

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). No 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 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.

Number of partners requesting funding	Possible number of additional partners with own funding
3	2
4	
5	
6	
7 (only possible with inclusion of Eastern European partner)	2
8 (only possible with inclusion of Eastern European partner)	2

Each transnational proposal must nominate a **project consortium coordinator** among the project partner principal investigators. The coordinator must be a project partner from an E-Rare-3 JTC 2016 funding country/region. The project coordinator will represent the consortium externally and towards the JCS and CSC, and will be responsible for its internal scientific management (such as controlling, reporting, intellectual property rights issues and contact with the JCS). Each project partner will be represented by a single principal investigator. Within a joint proposal, the principal investigator each project partner will be the contact person for the relevant country/regional funding organisation.

The duration of the projects can be up to 3 years. Nevertheless, a partner can receive funding for less than 3 years according to E-Rare-3 JTC 2016 funding organisations eligibility criteria and regulations.

The requested budget for the project should be adequate to the needs of the proposed work. Projects requesting a contribution in a range of 1 to 2M€ would be suitable. Nonetheless, this does not preclude submission and selection of a proposal requesting other amounts if justified.
Please check Annex II for further details regarding funding rules and requirements at national level.

4.2. Submission of joint proposals

Coordinators of a joint transnational proposal who want to submit a project to this call shall **pre-register online before 1st February 2016 at 05 p.m. GMT** by indicating the type of study (Type A or Type B – see description in section 2.) and the disease / group of diseases of interest in the project.
The link to the pre-registration portal is: https://www.pt-it.de/ptoutline/application/erare16

There will be a **two-stage submission/evaluation procedure:**
Stage 1: Submission of a full joint application
Stage 2: Submission of rebuttal/modified proposal

One joint full proposal document (in English) shall be prepared by the partners of a joint transnational proposal, and must be submitted to the JCS by uploading it on the electronic submission system by one spokesperson, the coordinator.

Joint **proposals** (in English) must be uploaded on the online submission system no later than **3rd March 2016 at 05 p.m. GMT**. The proposals should strictly follow the "Guidelines for applicants".
The link to the submission portal is: https://www.pt-it.de/ptoutline/application/erare16

The decision on selection of applications for invitation to the second stage of submission and evaluation will be communicated by mid-June 2016 (see also Paragraph 5: Evaluation).

Please note that **joint rebuttal / modified proposals will be accepted only from those applicants who were explicitly invited by the JCS to submit them.** Rebuttal / modified proposals (in English) must be submitted to the JCS in an electronic version no later than **18th July 2016 at 05 p.m. GMT**.

The final selection on proposals will be communicated to applicants as soon as possible and before the end of October 2016.

The submitted proposals have to respect the relevant international standards like: Declaration of Helsinki, ICH guideline for good clinical practice (ICH-GCP), EC directive 2005/28/EC, EU Regulation No. 536/2014, CONSORT-Statement, STARD.

Further information on how to submit proposals electronically will be made available through the E-Rare website (www.e-rare.eu) and in the "Guidelines for applicants". The forms that have to be used for submission of proposals are available on the E-Rare website. Applicants should take note of individual national/regional rules, and should contact their national/regional contact person for any questions (see "contact information" section).

For applicants from some countries/regions it might be necessary to submit the proposals and/or other information directly to the country/regional funding organisations. Therefore, applicants are strongly advised to contact their national/regional funding organisations for more details (see country/regional contact details and "Guidelines for applicants").

4.3. Further information

If you need additional information, please contact the JCS or your national/regional funding organisation representative (see contact information below). For further details please refer to the "Guidelines for applicants" or www.e-rare.eu. **The adherence to the national/regional regulations in the "Guidelines for applicants" document is mandatory.**

5. EVALUATION

5.1. Evaluation criteria

Proposals will be assessed according to specific evaluation criteria (see below), using a common evaluation form. A scoring system from 0 to 5 will be used to evaluate the proposal's performance with respect to the different evaluation criteria.

Scoring system:

0: Failure. The proposal fails to address the criterion in question, or cannot be judged because of missing or incomplete information.

1: Poor. The proposal shows serious weaknesses in relation to the criterion in question.
2: Fair. The proposal generally addresses the criterion, but there are significant weaknesses that need corrections.
3: Good. The proposal addresses the criterion in question well but certain improvements are necessary.
4: Very good. The proposal addresses the criterion very well, but small improvements are possible.
5: Excellent. The proposal successfully addresses all aspects of the criterion in question.

Evaluation criteria:

1. **Excellence**
    a. Clarity and pertinence of the objectives and of the hypothesis(es) at the base of the study;
    b. Soundness of the evidence presented in support of the medical need and of the study rationale;
    c. Innovation and relevance of the study in terms of potential clinical and public health impact;
    d. Competence and experience of participating research partners (previous work in the field, specific technical expertise) and complementarity within the consortium;
2. **Impact**
    a. Added-value of transnational collaboration: gathering a critical mass of patients/biological material, sharing of resources (models, databases, diagnosis etc.), harmonization of data, sharing of specific know-how and/or innovative technologies, etc. ;
    b. Potential of the expected results for commercial exploitation and for future clinical, public health and/or other socio-economic health relevant applications;
    c. Effectiveness of the proposed measures to exploit and disseminate the project results (including freedom to operate analysis and management of IPR), to communicate the project, and to manage research data where relevant;
    d. Involvement of pertinent patient organisation, patient representatives or industry (if available).
3. **Quality and efficiency of the implementation**
    a. Adequateness, coherence and feasibility of the study design to verify the hypothesis(es) and to respond to the medical need;
    b. Coherence and effectiveness of the work plan and study design (appropriateness of the allocation of tasks, resources, time-frame, infrastructural support to the clinical trial, documented feasibility of the recruitment and retention of patients to the study, etc.);
    c. Appropriateness of the management structures and procedures, including risk and innovation management;
    d. Budget and cost-effectiveness of the project (rational distribution of resources in relation to project's activities, partners responsibilities and time frame);
    e. Description of potential risks and how to handle them, including involvement of and charter for independent data monitoring and safety committee where relevant.
4. **Clinical aspects of the clinical trial**
    a. Sufficient evidence provided to justify a phase I/II clinical trial at this time including presentation of other existing trials addressing a comparable question (if applicable) and documentation of clinical safety of the Agent(s);
    b. Compliance with the regulatory requirements and adequateness of the consideration of the ELSI (Ethical, Legal and Social Implications) issues;

c. Relevance and adequateness of the outcome measures/endpoints with respect to the overall objectives of the trial;
d. Adequateness of the target and study population and of the controls and/or comparators;
e. Adequateness of the consideration of the potential clinical and epidemiological consequences of the trial results;

5. **Statistical and biostatistical aspects of the clinical trial**
   a. Adequateness of the randomisation criteria, if applicable;
   b. Adequateness of the assumptions underlying the sample size calculations, as substantiated by the literature;
   c. Adequateness of the proposed strategy for statistical and biostatistical analysis;
   d. Impact of non-compliance and missing values on the sample size.

Evaluation scores will be awarded for the 5 main criteria, and not singularly for the different aspects listed below the criteria. Each criterion will be scored out of 5.

5.2. Eligibility check of proposals and two steps peer review

5.2.1. Eligibility check

The JCS will check all proposals to ensure that they meet the call's formal criteria (date of submission; number and country distribution of participating research partners; inclusion of all necessary information in English, page length of each section). The JCS will forward the proposals to the CSC members who will perform a check for compliance to country/regional rules as described in the "Guidelines for applicants".

Please note that proposals not meeting the formal criteria or the national/regional eligibility criteria and requirements **will be declined without further review.**

5.2.2. First step of peer review of full proposals

Full proposals passing the eligibility check (call secretariat and country/region) will be forwarded to the SEC members and external reviewers for a first evaluation (see evaluation criteria above). The SEC members and external reviewers will perform the assessment of the proposal and fill the evaluation forms with scores and comments for each criterion. Each proposal will be assessed by 2-3 SEC members and 2 external reviewers. Each project will be reviewed by at least one methodology (CT) expert and one disease/medical domain specialist. Written reviews of external experts will be sent to the SEC members, who will meet in order to discuss each proposal and establish a list of proposals recommended for the second step. The CSC will meet to decide which proposals will be accepted for the rebuttal/modified proposal submission based on the recommendations issued by the SEC.

5.2.3. Rebuttal/modification stage

After the first step of evaluation of the proposals, evaluation reports including suggestions to improve the proposals will be sent to applicants accepted for this second stage. Each project coordinator will be provided with the opportunity of studying these assessments and commenting on the arguments and evaluations of the reviewers, which remain anonymous. This stage allows applicants to comment on factual errors or misunderstandings that may

have been committed by the reviewers while assessing their proposal and to reply to reviewers' questions (please see "Guidelines for applicants" for details). In addition, the applicants will have the possibility to modify the project description following the evaluation recommendations. However, the modifications of the work plan must be limited to the recommendations.

5.2.4. Formal criteria check of rebuttal / modified proposals

The JCS will check the modified proposals to ensure that they meet the call's formal criteria before sending them to the SEC members.

5.2.5. SEC evaluation

The JCS will send final proposals to the SEC members. The SEC will meet to discuss each proposal and, after consideration of the evaluation criteria, rebuttals and their own discussions, the SEC will make a classification of the proposals and rank proposals recommended for funding.

5.3. Funding decision

Based on the ranking list established by the SEC and on available funding the CSC will suggest the projects to be funded to the national/regional funding organisations and patient organisations that are interested to co-fund projects in their area of interest. Based on these recommendations, final decisions will be made by the national/regional funding organisations and patient organisations and will be subject to budgetary considerations.

If necessary, the CSC will determine a priority order for proposals, which have been awarded the same score within a ranked list. The following approach will be applied successively for every group of ex aequo proposals requiring prioritisation, starting with the highest scored group, and continuing in descending order:

- Availability of national funding;
- Maximisation of use of national funding;
- Proposals that address diseases not otherwise covered by more highly-ranked proposals.

The Joint Call Secretariat will communicate to all project coordinators the final decisions together with the review from the SEC.

6. FINANCIAL AND LEGAL ISSUES

6.1. Funding model

The E-Rare-3 JTC 2016 Funding Partners have agreed to launch a joint call using the "virtual common pot" funding mode. This means that national/regional funding will be made available through national/regional funding organisations according to national/regional funding regulations.

Each country/region funds only its national/regional component of the transnational research project. Eligible costs and funding rates may vary according to the corresponding national/regional funding organisation regulations. Prior to submitting a proposal, applicants should verify their eligibility and financial support and are recommended to contact their national/regional contact person (see national/regional contact details). Funding is granted for a maximum of three years according to national/regional regulations.

6.2. Involvement of patients organisations

EURORDIS is a non-governmental patient-driven alliance of patient organisations representing 692 rare disease patient organisations in 63 countries. Through their involvement and coordination, interested patient organisations with research funding mandates will have access to anonymised summaries of the proposed work so that they can evaluate the relevance to their mandate or pre-determined area of research interest. Patient organisations will develop an agreement with the funding agencies to potentially co-fund selected proposals. The applicants will have the possibility to indicate if they are interested in the potential co-funding by Patients Organisations.

6.3. Funding contracts

Each project includes several consortium members called research partners and one project coordinator. Each research partner (including the project coordinator) will have a separate funding contract/letter of grant according to national/regional regulations with the appropriate national/regional funding institutions.

Changes to the composition of research consortia or in budget cannot occur during the contract/letter of grant, unless there is a good justification. Any minor changes have to be well justified and the relevant funding organisations will decide upon the proper action to be taken. However, in case of major changes, an independent expert can be consulted to help with the final decision of the funding organisations. The research partners shall inform the JCS and the funding bodies of that project of any event that might affect the implementation of the project.

6.4. Research consortium agreement and ownership of intellectual property rights

The project consortium partners must sign a consortium agreement (CA) for cooperation addressing the issues given in "Guidelines for applicants" on consortium agreements (available on the E-Rare website). The research consortium is strongly encouraged to sign this CA before the official project start date, and in any case the CA has to be signed no later than six months after the official project start date. Please note that national/regional regulations may apply concerning the requirement for a CA (Please contact your national/regional contact point or check the country-specific information on the guidelines). Upon request, this consortium agreement must be made available to the concerned E-Rare-3 JTC 2016 funding organisations.

Results and new Intellectual Property Rights (IPR) resulting from projects funded through the E-Rare-3 Joint Transnational Call will be owned by the partners' organisations according to national/regional rules on IPR. If several participants have jointly carried out work generating new IPR, they shall agree amongst themselves (consortium agreement) as to the allocation of ownership of IPR, taking into account their contributions to the creation of those IPR as well as the European guidelines on IPR issues.

The results of the research project and IPR created should be actively exploited and made available for use, whether for commercial gain or not, in order for public benefit to be obtained from the knowledge created.

The funding partners shall have the right to use documents, information and results submitted by the research partners and/or to use the information and results for their own purposes, provided that the owner's rights are kept and taking care to specify their origin.

6.5. IRDiRC policies and guidelines

The project partners are expected to follow IRDiRC policies and guidelines and to participate in IRDiRC working groups. For more information see http://www.irdirc.org/.

7. RESPONSIBILITIES, REPORTING REQUIREMENTS AND DISSEMINATION

The **coordinators** of all the funded projects must submit **brief annual scientific project reports and a final scientific project report** (within six months of the end of the project) to FNRS, Belgium, which is responsible for monitoring the funded projects. All reports must be in English and use the common electronic reporting form that will be provided. The research partners are jointly responsible for delivering the reports, and FNRS will only accept reports delivered on behalf of the consortium, via the project coordinator.

If required, each participant should submit financial and scientific reports to their **national/regional funding organisations**, according to national/regional regulations. The progress and final results of each individual contract/letter of grant will be monitored by the respective national/regional funding organisations.

The coordinators and/or national/regional group leaders might be asked to present the results of their projects at an **intermediate and/or a final status symposium** organized by E-Rare. Project proposal budget should foresee these expenses accordingly.

Type A projects will be evaluated at the end of the first year of duration of the projects. A committee of experts will evaluate the results of the pre-clinical study as well as the updated project of clinical trial and decide whether the project can go to the clinical trial or not. The coordinators of Type A projects must submit a scientific project report at the end of the first year to ANR, France which will be responsible for organising scientific evaluation of those reports by reviewers.
Clinical trials in type A and Type B projects will comprise three milestones, which will be evaluated during the life of the project:

1- The project has all administrative and regulatory authorisations
2- The project has included 50% of patients
3- The project has finished inclusions and data are analysed

ANR will be responsible for organizing evaluation of those milestones. The completion of each milestone may be necessary to go through the next funding phase according to national rules.

Projects selected for funding shall (this is mandatory):

- Commit to register the trial in a public register (for example on Clinicaltrials.gov) before inclusion of the first patient.
- Commit to post trial results in a public register (for example Clinicaltrials.gov) one year after the trial is completed, i.e. last follow-up of the last patient for the primary outcome.

- Commit to draft a manuscript and publish results irrespective of findings.
- Commit to make raw anonymised data sets available to the scientific community upon request in line with national legal requirements.

Funding recipients must ensure that all outcomes (publications, etc.) of transnational E-Rare-3 projects include a proper acknowledgement of ERA-NET E-Rare-3 and the respective national/regional funding partner organisations.

8. CONTACT AND FURTHER INFORMATION

The JCS is set up at ANR (The French National Research Agency) to assist the CSC and the national/regional funding bodies during the implementation of the call. FNRS, Belgium, will be responsible for the follow-up phase until the funded research projects have ended. The JCS will be responsible for the administrative management of the call. It will be the primary point of contact referring to the call procedures between the research consortia, the funding organisations (CSC) and the peer reviewers. The project coordinator will be the person contacted by the JCS during the application procedure, so he/she must forward this information to the other participants.

Further information on the E-Rare-3 Project, the Call and the follow-up is available at the E-Rare website (www.e-rare.eu). It is advised to contact the national/regional contact person for any questions regarding the Call (please see national/regional contact details below).

ANNEX I. National/regional contact details

Country/ Region	Institution	Website	National/regional contact
Austria	FFG	https://www.ffg.at/seka	Dr. Corinna Wilken Österreichische Forschungsförderungsgesellschaft mbH (FFG) Sensengasse 1 1090 Wien, AUSTRIA Telefon +43 (0)5 7755 – 1317 E-Mail : Corinna.wilken@ffg.at
Austria	FWF	http://www.fwf.ac.at	Dr. Stephanie Resch Phone: +43 (1) 505 67 40-8201, E-mail: stephanie.resch@fwf.ac.at Dipl. Ing. Anita Stürtz Phone: +43 (1) 505 67 40-8206, E-mail: anita.stuertz@fwf.ac.at
Belgium (Flanders)	FWO	http://www.fwo.be/en/	Olivier Boehme +32 2 550 15 45 Toon Monbaliu +32 2 550 15 70 eranet@fwo.be
Canada	CIHR	http://www.cihr-irsc.gc.ca	Nathalie Gendron [1(613) 941-8596] Nathalie.Gendron@cihr-irsc.gc.ca
Canada, Québec	FRQS	www.frqs.gouv.qc.ca	Karine Genest (514) 873-2114, ext 1275 karine.genest@frq.gouv.qc.ca Anne-Cécile Desfaits (514) 873-2114, ext 1368 annececile.desfaits@frq.gouv.qc.ca
France	ANR	www.agence-nationale-recherche.fr/	Halftermeyer Juliane [+33 1 78 09 80 22] Julkowska Daria [+33 1 78 09 80 78] E-RareCalls@agencerecherche.fr
France	DGOS	http://www.sante.gouv.fr/innovation-recherche-clinique.html	Noël Lucas noel.lucas@sante.gouv.fr Hélène Coulonjou Helene.COULONJOU@sante.gouv.fr Ariane Galaup-Paci Ariane.GALAUPPACI@sante.gouv.fr

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Israel	CSO-MOH	www.health.gov.il	Avi Israeli [+ 972-2-5082156] avii@moh.health.gov.il Irit Allon [+972-2-5082167] Irit.allon@moh.health.gov.il
Italy	MoH	www.ministerosalute.it/	Dr. Gaetano Guglielmi- phone: +39 065994 2186. Head Office 3 (Health Research IRCCS), Directorate General for Health Research and Innovation Ministry of Health, Viale Giorgio Ribotta, 5. 00144 Rome, Italy E-mail:g.guglielmi@sanita.it
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ANNEX II. Indicative funding commitments of the participating organisations of the E-Rare-3 JTC 2016

Country/ Region	Participating organisation	Envisioned amount of funding (M€ for 3 years)	Anticipated number of fundable research partners
Austria	Austrian Research Promotion Agency (FFG)	2 (1)	4
Austria	Fonds zur Förderung der Wissenschaftlichen Forschung (FWF)	0,5	2
Belgium (Flanders)	Research Foundation – Flanders (FWO)	0,2	1
Canada	Canadian Institutes of Health Research (CIHR)	2,5 (2)	4
Canada, Québec	Fonds de recherche du Québec - Santé (FRQS)	0,36	1-2
France	Agence Nationale de la Recherche (ANR)	1 (3)	4 (4)
France	Ministère des Affaires sociales, de la Santé et des Droits des femmes (DGOS)	1,5 (5)	-
Germany	German Federal Ministry of Education and Research (BMBF)	3	8 to 10
Germany	German Research Foundation (DFG)	1,5	5
Hungary	National Research, Development and Innovation Office (NKFIH)	0,15	1 or 2
Israel	Chief Scientist Office of the Ministry of Health (CSO-MOH)	0,2 (6)	up to 2
Italy	Italian Ministry of Health (MoH)	1	4-6
Latvia	State Education Development Agency (Valsts izglītības attīstības aģentūra VIAA)	0,3	1-2
Poland	Narodowe Centrum Badań i Rozwoju (NCBR)	0,4	1-3
Portugal	Foundation for Science and Technology (FCT)	0,25	1-2
Spain	National Institute of Health Carlos III (ISCIII)	0,25 (7)	2-3
Switzerland	Swiss National Science Foundation (SNSF)	0,9	3 to 4
Turkey	The Scientific and Technological Research Council of Turkey (TUBITAK)	0,6	4-5

(1) If Austrian project activities primarily involve experimental development aspects they will be founded mainly with a grant, otherwise they will be funded with convertible loans.
(2) In Euros, including federal partners but excluding FRQ-S
(3) ANR will only fund the pre-clinical part of projects.
(4) Maximum funding of 250 000€ per project.
(5) DGOS will only fund clinical trials.
(6) CSO-MoH will only fund the pre-clinical part of projects.
(7) Up to 100.000 € per partner (overheads included), up to 150.000 € per coordinator (overheads included)

ANNEX III. Eligibility of beneficiary institutions for the participating organisations of the E- Rare-3 JTC 2016

Country/ Region	Institution	Eligible benificiary institution		
		Academia	Clinical/ public health	Company
Austria	Austrian Research Promotion Agency (FFG)	No	No	Yes (1)
Austria	Fonds zur Förderung der Wissenschaftlichen Forschung (FWF)	Yes (2)	Yes (2)	Yes (2)
Belgium (Flanders)	Research Foundation – Flanders (FWO)	Yes (3)	Yes (3)	No
Canada	Canadian Institutes of Health Research (CIHR)	Yes	Yes	No
Canada, Québec	Fonds de recherche du Québec - Santé (FRQS)	Yes	Yes	No
France	Agence Nationale de la Recherche (ANR)	Yes	Yes	Yes (4)
France	Ministère des Affaires sociales, de la Santé et des Droits des femmes (DGOS)	No	Yes	Yes (5)
Germany	German Federal Ministry of Education and Research (BMBF)	Yes	Yes	Yes
Germany	German Research Foundation (DFG)	Yes	Yes	No
Hungary	National Research, Development and Innovation Office (NKFIH)	Yes (6)	Yes (6)	No
Israel	Chief Scientist Office of the Ministry of Health (CSO-MOH)	Yes	Yes	No
Italy	Italian Ministry of Health (MoH)	No	Yes (7)	No
Latvia	State Education Development Agency (Valsts izglītības attīstības aģentūra VIAA)	Yes	Yes	Yes (8)
Poland	Narodowe Centrum Badań i Rozwoju (NCBR)	Yes	Yes	Yes
Portugal	Foundation for Science and Technology (FCT)	Yes	Yes	Yes (9)
Spain	National Institute of Health Carlos III (ISCIII)	Yes (10)	Yes	No
Switzerland	Swiss National Science Foundation (SNSF)	Yes	Yes	No
Turkey	The Scientific and Technological Research Council of Turkey (TUBITAK)	Yes	Yes	No

(1) up to 60% of total eligible costs if experimental development aspects are dominating, otherwise up to 50% as convertible loan
(2) Applications for projects from FWF (Austria) may only be submitted by single natural persons. Affirmation of the research institution (academia, clinical/public health, enterprise) of the applicant is mandatory.
(3) Only clinics or Belgian scientific institutions (Dutch language framework) associated with universities are eligible for the FWO.
The eligibility of companies and institutions is subjected to different conditions in each country/region. Further details regarding the eligible beneficiaries and other national/regional eligibility criteria and requirements are available on the "guidelines for applicants" and the E-Rare website (www.e-rare.eu).

(4) The eligibility of companies and institutions is subjected to different conditions in each country/region. Further details regarding the eligible beneficiaries and other national/regional eligibility criteria and requirements are available on the "guidelines for applicants" and the E-Rare website (www.e-rare.eu).
(5) The eligible benificiaries are healthcare facilities
(5) Companies may be eligible if other institutions as healtcare facilities are also funded
(6) Further details regarding the eligible beneficiaries and other national eligibility criteria and requirements are available on the "guidelines for applicants" and the E-Rare website (www.e-rare.eu).
(7) Scientific Institutes for Research, Hospitalization and Health Care (Istituti di Ricovero e Cura a Carattere Scientifico pubblici e privati, IRCCS)
(8) Must comply with regulation 651/2014
(9) Up to 50% of the total eligible costs
(10) Academic research groups belonging to CIBER, CIBERNED, EU-Openscreen preparatory phase (ChemBioBank Network) and accredited Health Research Institutes (IIS). Further details available on "guidelines for applicants" and the E-Rare website (www.e-rare.eu).