Federal Ministry of Education and Research

Announcement

CALL FOR PROPOSALS FOR CONFIRMATORY PRECLINICAL STUDIES

- QUALITY IN HEALTH RESEARCH -

10. December 2018

1 Objective, purpose, legal basis

1.1 Objective and Purpose

For people's health care, new therapies and better and safer drugs are needed. To this end, promising therapeutic approaches and drug candidates must be identified in pre-clinical studies and then validated. For these to be reliable in subsequent clinical development, preclinical results must be predictive, replicable, and backed by appropriate quality standards and validation procedures.

The aim of this funding measure is to strengthen preclinical research and its transfer of results. The evidence, robustness and reliability of science-initiated preclinical research should be increased. For this purpose, science-initiated confirmatory studies should be funded. The research results obtained in these studies should have a high relevance for medical care in Germany. They should be suitable to be transferred in a next step to further preclinical development and then to early clinical trials.

The framework program Health Research of the Federal Government pursues the goal of accelerating the transfer of research findings into application (Translation). As a contribution to the implementation of this goal, the Federal Ministry of Education and Research (BMBF) is promoting the bridging between biomedical laboratory research and preclinical or clinical development with this funding measure. The BMBF is taking up a recommendation from the Health Research Forum on "Overcoming the hurdles in the value-added chain in health research".

2 Object of funding

The funding measure is divided into the following modules:

<u>Module 1: Confirmatory Preclinical Studies</u>

Science-initiated, prospective, controlled preclinical studies to prove the efficacy of a clinically relevant therapeutic approach should be funded. These confirmatory studies are intended to validate the findings of exploratory studies. It is to be examined whether the results are suitable for subsequent further preclinical development steps and a transfer into clinical studies or whether further fundamental research is necessary. To ensure efficient transfer of preclinical outcomes into the application, it is important to ensure that partners in a

research network with demonstrable expertise in the development and exploitation of new therapies are involved. The prospects for clinical feasibility and perspectives for commercialization of the therapeutic approach must be in place.

In the exploratory studies, the proof has been furnished that an active substance or a therapeutic procedure manipulates the target structures in the desired sense. The quality of the exploratory study results and other preparatory work must justify the confirmatory study.

The validation of a promising therapeutic approach in a confirmatory preclinical study must be carried out in models of disease that are relevant to the respective human diseases and that allow predicting the efficacy of the substance or process. Each study must have a confirmatory goal with carefully planned study design, adequate procedures to reduce bias, and statistical sample size calculation. For this purpose, appropriate biometric expertise has to be integrated into the project. The studies should preferably be carried out as multicentric studies. Appropriate measures must be taken to ensure the independence of the study management and the data analysis. Monocentric confirmatory preclinical studies can only be funded in justified exceptional cases.

The BMBF intends to avoid animal experiments wherever possible. For this reason, projects are to be promoted here that use corresponding alternative methods.

Module 2: Systematic reviews and meta-analyzes

Funding will be provided for systematic reviews and meta-analyzes of preclinical studies in a specific disease area. International standards for the analysis of the evidence of preclinical research are to be observed.

Module 3: Scientific accompanying Project

An independent scientific accompanying project is to be funded. The accompanying project should support the methodological quality of the projects during their lifetime. The challenges and special features of the preclinical confirmatory studies as well as systematic reviews and meta-analyzes are to be comprehensively addressed. For this, it is necessary that own previous achievements exist on this subject. In addition, it must be ensured that partners are involved who have proven expertise in the development and exploitation of new therapies. The results and experiences from the projects are to be evaluated comprehensively and used to further develop the methodology of preclinical confirmatory studies. The results of the accompanying project are to be prepared in a guideline and made available to academic groups and research institutions. The funded projects should be included in the development of the guideline in an iterative process. A broad and sustainable scientific use of the guideline should be ensured through i.a. publications, training programs and an online expert platform.

3 Funding recipients

Eligible applicants are state and state recognized universities and non-university research institutions as well as companies in the commercial sector. At the time of disbursement of a granted grant, the presence of a place of business or establishment (company) or other entity serving the grant recipient (state and non-governmental and non-university research institutions) is required in Germany.

4 Special Funding Requirements

With the funding requirements listed below, the BMBF aims for valid and reliable results of the funding measure. For research results to be translated into subsequent steps in the translation chain, they must be scientifically robust, valid and fully published. Research funding must therefore pursue the criteria of relevance, stringent research methodology and transparent publication practice.

Previous achievements

Applicants must be qualified by relevant previous achievements. This applies in particular with regard to preclinical research methodology (including study design for preclinical studies as well as systematic reviews and meta-analyzes). The envisaged investigation methods must already be successfully established when the application is submitted. In pre-clinical confirmatory studies (Module 1), relevant preliminary work on the clinical picture is required. The relevance of the models to be used for the confirmatory studies for the respective clinical picture must be sufficiently proven.

The infrastructure required to carry out the project is required. The expertise and capacities required for the respective research goals have to be adequately integrated into the projects. In the case of confirmatory preclinical studies (Module 1), applicants must, at the time of application, research the patent situation for the treatment or substance presented in the application, describe it in the application and safeguard IPR on the results worthy of protection accordingly.

Collaboration

If partners join together to form a joint project, a coordinator must be nominated. The partners of a joint project regulate their cooperation in a written cooperation agreement. … Active collaboration of all grant recipients with the accompanying project is expected.

Scientific standards

Applicants are required to comply with national and international standards for quality assurance of preclinical research. GCCP and the ARRIVE Guidelines are to be considered in Module 1 as amended. For systematic reviews and meta-analyzes (Module 2), the tools and notes of "SYRCLE" as well as the PRISMA Reporting Guidelines should be considered.

Quality of the methods used

Prerequisite for funding is a high quality of the methodology of the proposed project. When planning the project, the national and international state of research must be adequately taken into account. The validity of the investigation procedures must be ensured in relation to the chosen research question. The continuous integration of biometric and other methodological expertise into the project must be ensured.

Accessibility and long-term assurance of research data and results

Access to scientific findings and data is an essential foundation for research, development and innovation. The long-term safeguarding and provision of research data contribute to the traceability and quality of scientific work. Therefore the following conditions apply:

- The registration of confirmatory preclinical studies and systematic reviews and meta-analyzes in appropriate registries is recommended.

- Data management plans should be prepared and submitted.

- Research results generated under this funding directive must be published, even if the study hypothesis has not been confirmed (NULL results).

- The publication of the study results should principally be done as an open access publication (see also number 6).

- Original data on the publications should be made available for subsequent use (digital, while respecting the rights of third parties, in particular data protection, copyright).

Further details are available in the guideline to this funding directive.

Exploitation and use possibilities

The expected results must provide a concrete insight for future therapeutic developments. The planned exploitation, the transfer of the results into further development steps as well as strategies for sustainable implementation must be addressed in the conception of the requested project and described on a structural and procedural level.

5 Nature and extent, amount of the grant

The grants are granted through project funding.

Confirmatory preclinical studies (module 1) can usually be funded for a period of up to three years, systematic reviews and meta-analyzes (module 2) for a period of two years, the accompanying project can be funded for a period of four years. An interim evaluation is planned for the accompanying project after two years.

Eligible for non-commercial applicants is the project-related extra work, such as personnel, material and travel expenses, and in justified exceptional cases, project-related investments that are not included in the basic equipment of the applicant (s). In addition, expenses / costs are eligible for the following items:

a) Execution of research projects

- Expenses for the preparation of the detailed study protocol;
- Expenditure for registering the study or the systematic review, for monitoring or advice on quality assurance;
- Spending on the introduction of quality assurance measures such as the validation of reagents, biologics, cell lines and model systems, electronic laboratory notebooks, structured documentation and storage of data, and travel expenses for meetings and workshops for cooperation with the scientific support project;
- Expenditure on publication fees incurred for the open access publication of the project results during the term of the project can be reimbursed;
- Contributions to the membership in the `Technologie und Methodenplattform für vernetzte medizinische Forschung (TMF eV, see http://www.tmf-

ev.de/Mitglieder/Mitglied_werden.aspx), if the TMF membership serves the project progress and thus the achievement of this project;
- Rotation positions for clinical scientists who are to be exempted for a limited period of time from their routine care work and who need to be replaced.

b) Coordination and services

- The preparation of project-specific research data for re-use by other scientists (open data), infrastructure and personnel costs for the controlled release of data and for the transfer into existing data infrastructure, e.g. site or topic databases can be funded.

c) International cooperation

- Cooperations with thematically related R & D projects in European and non-European countries are possible, whereby the international partner must in principle have its own national funding for his project share. Additional resources, e.g. for scientific communication, for workshops and work meetings, guest stays of junior scientists and scholars (postgraduates, post-docs) from the network at external research facilities and clinics as well as the invitation of guest scientists are eligible for funding if synergistic effects can be expected thereby;
- If cooperation with a foreign working group is necessary for the processing of a substantial subproject, personnel and material resources in the form of a subcontract are eligible. Existing needs and scientific added value must be justified.

… (admin. details)