NCATS

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Drug Development Collaboratory (UG3/UH3)

PAR-20-301

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NCATS Overview

- The National Center for Advancing Translational Sciences (NCATS) was established to transform the translational science process so that new treatments and cures for disease can be delivered to patients faster.

Drug Development Collaboratory

- The Drug Development Collaboratory is designed to enhance synergies across NCATS intramural laboratories and extramural programs to build a more comprehensive therapeutic development path than either arm of NCATS can provide alone.
- The Collaboratory represents a partnership between multiple programs and divisions with shared interests to advance novel therapeutic candidates into clinical testing.

Purpose

- To support translational science collaborations between extramural researchers and the scientists of the intramural NCATS Therapeutic Development Branch (TDB).
- Collaborations will focus on completing the late-stage preclinical development of new therapeutic candidates – including small molecules, biologics and gene therapies – and transitioning them to clinical evaluation.

NCATS TDB: https://ncats.nih.gov/about/center/org/dpi/collaborate#late-stage-translation

Collaboration with Intramural NCATS Scientists

- This FOA requires partnerships with the intramural investigators of the NCATS Therapeutic Development Branch (TDB) to advance novel therapeutic candidates into clinical evaluation.
  - TDB scientists are experts in preclinical therapeutic development.
  - A wide range of therapeutic indications may be proposed for collaboration.
- Applications require a formal Collaboration Plan, negotiated in advance with NCATS TDB, outlining the studies to be completed and articulating which will be conducted at NCATS and which will be conducted by the applicant investigator.

Research Scope

- The objective of this FOA is to support translational science collaborations between extramural researchers and NCATS intramural scientists.
  - This FOA represents a bridge between the late-stage preclinical development of novel therapeutic candidates and their early clinical evaluation, providing continuity of support once an Investigational New Drug (IND) application is cleared by the FDA.
  - Preclinical development is conducted in collaboration with the intramural scientists in the NCATS Therapeutic Development Branch.
  - Early-stage clinical trials will be conducted at the applicant institution with support from the extramural NCATS Drug Development Partnership Programs.
- Collaborations can include, but are not limited to, optimization of drug delivery strategies; optimization of drug formulation; design and execution of preclinical studies necessary to enable clinical evaluation; and clinical trial design and site-readiness activities.

Activities Considered Out of Scope

- Examples of activities that are non-responsive to this FOA and that will not proceed to peer review:
  - Projects that do not already have efficacy data for the indication or that do not document evidence that efficacy data are not required for regulatory approval.
  - Projects that have not identified the lead candidate for IND-directed development or that would require additional optimization (e.g., medicinal chemistry).
  - Projects that seek to make only incremental improvements upon the characteristics of an existing therapy (e.g., improved pharmacokinetics) or that would be a follow-on to current effective standard(s) of care.
  - Projects that do not include in their application a Collaboration Plan previously negotiated with the NCATS Therapeutic Development Branch.
  - Projects that propose testing the effectiveness of a dietary supplement.
  - Applications that propose Phase III clinical trial activities for a common disease or condition.

Entry Criteria

- Projects must meet the following requirements prior to applying:
  - The applicant must have rigorous and sufficient efficacy data in the most relevant disease models before requesting a partnership with NCATS intramural scientists.
- Preparatory Activities for the UG3 Phase
  - **Partnering Request:** the applicant must initiate a Partnering Request to the NCATS Therapeutic Development Branch (TDB) at least ***16 weeks*** prior to preparing an application to learn more about the intramural partnering process (askTDB@nih.gov). The request to TDB must include a 2-page project summary. Refer to the section labelled "Partnering Request with NCATS Intramural" in this funding opportunity announcement for more information. Both a Collaboration Plan and a Letter of Support from the NCATS Scientific Director must be included for the application to be complete.
  - **Collaboration Plan:** the applicant must describe the partnership with NCATS TDB in a Collaboration Plan that will be included in the application.
  - **Letter of Support:** the applicant must obtain a Letter of Support signed by the NCATS Scientific Director that will be included in the application.
  - **For Phase III Clinical Trial or Equivalent for a Rare or Neglected Disease:** Consultation with NCATS extramural program official at least 10 weeks prior to the application due date is strongly encouraged (for both new and resubmission applications). If a project proposes the equivalent of a phase III clinical trial for a rare disease, a letter must be obtained from the NCATS program official, confirming whether the indication meets the definition of a rare and neglected disease.

Preparatory Activities for the UG3 Phase

- The applicant must initiate a Partnering Request to the NCATS Therapeutic Development Branch (askTDB@nih.gov) at least ***16 weeks*** prior to preparing an application. This requires submission of a structured summary of the proposed project, not to exceed two pages.
  - This summary should describe the therapeutic agent, the disease, the goals for improved therapies, the available efficacy and safety data in the disease-relevant models, and the particular NCATS resources necessary to advance the project to a successful regulatory filing stage. The narrative should not include proprietary, confidential information or trade secrets, but should be generally informative to persons working in related fields.
- During this engagement, TDB scientists will:
  - Determine whether the project is a strategic fit with the NCATS intramural mission.
  - Determine whether the intramural program has the capacity and bandwidth to collaborate on the specific project goals.
- After initial discussion, applicants with projects within the strategic fit for NCATS intramural will be expected to provide a more detailed project description, expanding on the content of the initial non-confidential summary. This description may require provision of non-public information and if so, applicants will be expected to sign a two-way Confidential Disclosure Agreement (CDA).
  - Learn more: https://ncats.nih.gov/alliances/forms
- If TDB determines that a project is a strategic fit and that there is sufficient capacity to collaborate, a Collaboration Plan will be developed outlining what experiments will be conducted at NCATS and what experiments will be conducted by the applicant.

UG3 Phase

- Supported partnerships will generate data and materials necessary for the filing of an IND application with the FDA.
- The UG3 phase will provide funding to the external partner *only* for those activities to be conducted *by* the applicant.
  - Work conducted by the TDB scientists is supported by intramural NCATS funds.
  - The applicant may only request support for those activities to be conducted by the applicant, not the activities to be conducted by the intramural NCATS scientists.
- Participation of the NCATS scientists is limited to the UG3 phase only.
- If UG3 milestones are met and an IND is cleared, support may be provided for an early-stage clinical trial in the UH3 phase.

UH3 Phase

- Funding for the clinical UH3 phase is contingent upon successfully meeting the milestones in the preclinical UG3 phase.
- NCATS strongly encourages applicants to involve patients or their representatives in the planning of the clinical trials, as appropriate.
- The initial application is expected to provide quantifiable milestones to determine success of the clinical UH3 phase.

Project Areas of Interest

- Activities for the UH3 may include:
  - *Phase I Clinical Studies:* Studies conducted in the target patient population and with healthy volunteers, where the purpose is to evaluate safety, determine a safe dose range, and identify side effects prior to conducting a Phase II clinical trial.
  - *Phase II Clinical Studies:* Studies conducted in a larger patient population, which typically enroll 150 subjects or fewer for trials in adults. The purpose of the Phase II clinical study is to demonstrate efficacy in the target population.
  - *Clinical Trials for Rare Disease:* Due to small numbers of available patients, the terms Phase I, Phase II and Phase III clinical trials may not always be appropriate. Therefore, well-controlled studies in a rare disease population may be proposed. The purpose is to demonstrate substantial evidence of efficacy in treating or preventing the condition, and to establish evidence of safety for that use.
  - Evidence of efficacy for a rare disease may be established in one or more adequate and well-controlled clinical trials in the identified population.
    - For more information, see Rare Disease: Common Issues in Drug Development Guidance for Industry: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM458485.pdf)

Research Areas of Interest

- Key priorities of this FOA are as follows:
  - Projects with the potential to address system-wide bottlenecks in the translational science research process.
  - Projects that use or seek to develop broader platform technologies that could subsequently be applied to benefit other disease areas.
  - Drug repurposing or repositioning studies.
  - Projects testing novel drug delivery strategies and testing optimal formulation strategies of commercially available assets that have been publicly posted on open innovation websites.
  - Clinical trials that test more than one related disorder at the same time. Patient population selection strategies that are similar to the basket approaches being tried in cancer research are of interest for rare and neglected disease studies when shared pathways are involved in the disease progression and the endpoints are the same or similar.

Prior Consultation

- Potential applicants are *strongly encouraged* to consult with NCATS Extramural Program Staff (Newtherapeuticuses@nih.gov) in the New Therapeutic Uses for Existing Molecules program early in the planning of an application. This early contact will provide an opportunity to discuss and clarify NIH policies and guidelines, including the scope of the project and intent of this FOA.
- Potential applicants are **required** to discuss their proposed projects with the NCATS Therapeutic Development Branch (askTDB@nih.gov) in advance.
  - A complete application **requires** a letter of support from the Scientific Director of the NCATS Division of Preclinical Innovation (DPI) that documents agreement of NCATS scientists to participate in the proposed collaboration.

Budget and Project Period

- Application budgets are not limited but must reflect the actual needs of the proposed project.
- The applicant may only request support for those activities to be conducted by the applicant, not the activities to be conducted by the intramural NCATS scientists.
- The project period is limited to 3 years for the UG3 phase and 4 years for the UH3 phase.
- The maximum project period is 7 years.

Application Instructions

- The definitive source of information for this initiative is the Funding Opportunity Announcement (FOA) https://grants.nih.gov/grants/guide/pa-files/PAR-20-301.html and any Notices referenced therein.

- Applicants should read all instructions in the FOA before preparing an application.

Q & A

Are there specific diseases or conditions of interest to NCATS and the Therapeutic Development Branch?

- NCATS works broadly across therapeutic areas and does not focus on a specific organ, system, or family of diseases. Rather, NCATS and the Therapeutic Development Branch prioritize rare diseases generally, with a specific focus on those conditions that lack effective treatments.
  - NCATS considers rare diseases as defined by the FDA Office of Orphan Products Development and the Orphan Drug Act (i.e., affecting fewer than 200,000 patients in the U.S.).

Can I apply for a Phase III clinical trial for a common disease?

- No. NCATS is not able to support a Phase III clinical trial for a common disease.
  - For more information, see National Center for Advancing Translational Sciences (NCATS) Policy for Support of Phase III Clinical Trial Activities for a Rare Disease or Condition: https://grants.nih.gov/grants/guide/notice-files/NOT-TR-18-025.html

This UG3/UH3 is a Cooperative Agreement. What does that mean?

- Research Project Cooperative Agreement:
  - Supports discrete, specified, circumscribed projects to be performed by investigator(s) in an area representing their specific interests and competencies.
  - A support mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, NIH scientific or program staff will assist, guide, coordinate, or participate in project activities. See Section VI.2 for additional information about the substantial involvement for this FOA.

- Reference: https://www.niaid.nih.gov/grants-contracts/closer-look-cooperative-agreements

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