

**Proposal Instructions**  
**Bridging Interventional Development Gaps (BrIDGs) Program**  
*Division of Pre-Clinical Innovation (DPI)*  
*National Center for Advancing Translational Sciences (NCATS)*  
*National Institutes of Health (NIH)*

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***Introduction to BrIDGs***

Promising ideas for therapeutic interventions can encounter roadblocks in the pipeline for pre-clinical development. Translation can be facilitated by partnering with the private sector, but high-risk ideas or therapies for uncommon disorders frequently do not attract investment. When funding for new therapies is limited or not available, resources provided by the federal government can bridge the gap between discovery and clinical testing so that translation can occur.

Staff from the NCATS [BrIDGs program](#) collaborate with researchers in need of pre-clinical therapeutics development expertise and resources for the advancement of candidate therapeutics. The program's goal is to generate data and clinical-grade material for use in Investigational New Drug (IND) applications with a regulatory authority such as the Food and Drug Administration (FDA).

BrIDGs is not a grant program. Instead, researchers submit proposals to partner with NCATS intramural scientists. NCATS staff and its collaborators work together to create a product development plan and conduct late-stage pre-clinical studies. Studies are completed using the contract resources of NCATS and the National Cancer Institute under the direction of BrIDGs staff. NCATS and collaborating NIH Institutes and Centers provide contract funding. BrIDGs staff accept collaboration proposals on a rolling basis.

Public reporting burden for this collection of information is estimated to average one hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive, MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-0658). Do not return the completed form to this address.

## Scientific Expertise and Capabilities

NCATS is interested in proposals to develop the following types of therapeutic agents:

- Small molecules
- Peptides
- Oligonucleotides
- Gene vectors
- Recombinant proteins
- Monoclonal antibodies

Available expertise and resources include:

- Synthetic process development
- Scale-up and manufacture of active pharmaceutical ingredients
- Development of analytical methods
- Development of suitable formulations
- Pharmacokinetic (PK) and absorption, distribution, metabolism and excretion (ADME) studies, including bio-analytical method transfer and validation
- Range-finding initial toxicology
- IND-directed toxicology
- Manufacture of clinical trial supplies
- Product development planning and advice in IND preparation

## Program Scope

Investigators may submit proposals to develop potential therapies for any disease or disorder. Be sure to obtain data from the most relevant *in vivo* models available before proposing to collaborate. Efficacy should be demonstrated via the intended clinical route of administration and preferably be published in a peer-reviewed journal or independently replicated. If efficacy has been demonstrated by a route which differs from that proposed for initial clinical trials, then additional data obtained by the different routes should be provided to compare exposure levels in target organs. Projects requiring earlier-stage resources, including assay development, high-throughput screening, medicinal chemistry optimization or additional *in vitro/in vivo* efficacy testing are not appropriate for BrIDGs and are out of scope.

Researchers interested in these resources should consider other programs within the [NCATS Division of Pre-Clinical Innovation](#) or consult with extramural program staff at the appropriate NIH Institute or Center to discuss other funding options.

In general, manufacture of clinical trial material for any type of agent will be limited to supplies for Phase I trials. Proposals to develop material for Phase II trials will be considered on a case-by-case basis. NCATS is not authorized to support Phase III research and will not consider requests for Phase III support.

Toxicology studies in support of Phase II or later trials (including carcinogenicity and reproductive toxicity studies) are outside of the scope of the program.

Regulatory affairs support is not offered by BrIDGs. Collaborators must identify other resources for preparing their IND, if required.

Funding for clinical trials of any phase is not available.

Vaccines, devices and diagnostic agents are ineligible for the program.

## Eligibility

BrIDGs collaborates with academic institutions, not-for-profit organizations, government laboratories, and Small Business Innovation Research (SBIR)-eligible businesses. View the [SBIR eligibility criteria](#). Foreign academic and nonprofit institutions may collaborate with BrIDGs. Foreign businesses are not eligible.

## **Confidentiality**

Information provided to BrIDGs is considered confidential. If BrIDGs seeks an opinion on the scientific merit of the project from external drug development experts, it will be done under conflict of interest and confidentiality agreements.

## **Material Transfer**

The output of BrIDGs program activities will be made available to the awarded institution in support of additional studies, an IND application, or performance of clinical trials. Data and products will be transferred to the institution under the terms of a collaboration agreement. View the [NCATS standard forms and model agreements](#).

## **Intellectual Property**

NCATS staff expect the originating investigator institution or a collaborating partner to have acquired or be in the process of acquiring appropriate protection for pre-existing intellectual property (IP) prior to contacting the program.

Under the Bayh-Dole Act, government contractors may elect to retain rights for a contribution they make during a BrIDGs collaboration that rises to the level of invention. However, BrIDGs contractors or subcontractors are generally subject to a [Determination of Exceptional Circumstances](#), through which their rights in subject inventions are assigned to the federal government. If NIH does file a patent application, the collaborating institution of record may be given the opportunity to negotiate an exclusive license under procedures set forth in [37 CFR Part 404](#).

To obtain this licensing opportunity, institutions must enter into a formal collaboration agreement prior to the initiation of a partnership with BrIDGs. Please see the NCATS [Forms and Model Agreements](#) page for a list of agreement templates.

## **Proposal Information**

The BrIDGs proposal process involves three steps.

The first step is to register with the proposal management website, [proposalCENTRAL](#). Registration in response to this opportunity is followed by the provision of a project abstract. The abstract must summarize the proposed collaboration in a way suitable for public dissemination. The text should describe the therapeutic agent, the disease, the goals for improved therapies, the available efficacy and safety data, and the request for BrIDGs expertise and resources. It should be informative to other persons working in the same or related fields and insofar as possible understandable to a scientifically or technically literate lay reader. Do not include proprietary information, confidential information or trade secrets in the description. If the proposal is approved, the abstract text may be publically used on the BrIDGs website and in other public NIH databases.

After registration, the second step in the process is to schedule a mandatory pre-proposal call with BrIDGs program staff. The purpose of the call is to assess project eligibility and orient investigators to the proposal and collaboration processes.

Once eligibility for the program has been confirmed, the final step in the process is to electronically submit a formal proposal via [proposalCENTRAL](#). The BrIDGs proposal consists of both a research description and required appendices.

## **Research Description**

The description should not exceed five pages (Arial 11pt, single space, 1" margins). Graphs, pictures and tables should be included in the body of the text and will count against the page limit. The description should explain the rationale for the development of the proposed agent and summarize the current stage

of its development. Manuscripts and supporting publications may be uploaded in the appendix to provide additional data. The following information should be provided in the research description:

### **Background**

Provide a brief summary of the disease to be treated. Discuss the current standard of care for the disease and why new therapies are needed. Explain the selection of, and level of agreement in the field regarding, the therapeutic target and its potential clinical relevance. Describe the proposed agent, its impact on the target and the rationale for selecting the agent over similar entities. Briefly describe the competitive landscape and the effectiveness of comparator compounds, if any.

### **Available Data**

As appropriate for the stage of the program, please describe data obtained to date in the areas below. Additional data can be submitted via the Data Collection Tables located in the Appendix to the [proposal template](#). Conclusive statements in the proposal should be backed by data provided in this section or in the appendix via the Data Collection Tables and the References section.

### **Chemistry**

- Medicinal chemistry optimization performed, including identified issues with the proposed molecule
- Acquisition of bulk substance (Good Manufacturing Practices [GMP] and non-GMP), process development efforts, and availability of protocols for scale-up production and analytical methods
- Development of suitable formulations, including drug concentrations and vehicles evaluated
- Production and stability assurance of dosage forms

### **PK/PD/Toxicology**

- Evaluation of PK and pharmacodynamics (PD), including bioavailability and half-life in serum and other relevant fluids/tissues
- The applicability of PD measures in animals as biomarkers in human studies
- Evaluation of ADME properties *in vitro* and *in vivo*, including routes and products of metabolism, microsomal stability, and related studies
- *In vivo* efficacy evaluation, including dosing and schedules
- *In vitro* and *in vivo* toxicology studies in rodents and non-rodents, including IND-directed toxicology

### **Regulatory Affairs and Clinical Trial Information**

- Potential clinical trial designs, including projected dose, dose regimen, length of treatment and duration of therapeutic response in humans, if known
- Determination of clinical endpoints and whether these are acceptable to regulatory agencies
- Results of consultations with FDA or other regulatory agencies, if any, on the project
- For repurposing projects in which clinical data are available:
  - Provide a summary of clinical efficacy, safety and PK/PD data.
  - Describe the clinical trial strategy, such as primary and secondary study objectives, endpoints, patient population, eligibility criteria, estimated sample size, treatment arms/regimens, statistical endpoints, correlative studies and patient samples required to perform correlative studies.
  - Describe availability of clinical trial support, infrastructure resources, and experts. If available, the Investigator's Brochure should be uploaded in the appendix.

### **Development Plans**

Provide a clear statement of the available BRIDGs expertise and resources that are requested as part of the proposed collaboration. If the investigator or their collaborator intends to conduct tasks that may affect research supported by the program (e.g., the investigator will provide the active pharmaceutical ingredient to NCATS for use in BRIDGs-supported studies), then the investigator should indicate how those tasks will be funded and conducted (including material quality and quantity).

Describe the status of any pending grant or resource applications that would lead to support for project tasks. This includes a summary of the status of past, planned or ongoing negotiations with companies related to licensure or future development of the product. Indicate how the BrIDGs collaboration would complement, not duplicate, other sources of support. For projects close to clinical application (e.g., solely clinical trial material or Good Laboratory Practice [GLP] toxicology studies are requested from BrIDGs), the investigator should document the strategy for obtaining funding for early phase clinical testing. Include potential collaborators and institutional arrangements for oversight and institutional review board review, if applicable. Provide letters of commitment from potential clinical investigators affiliated with the project.

### **Justification**

Briefly indicate why private funding for the project is not currently available. Describe the likelihood of the adoption of the therapeutic agent once an IND is cleared and why organizations (i.e., biotechnology companies, venture capital firms, pharmaceutical companies) are presently unwilling to fund or develop this project as it currently stands.

### **Required Appendices**

The following appendices are not page limited. Required appendices are indicated as such when applicable.

#### **1. Data Tables (Required)**

Tables are appended to the proposal template to facilitate data collection on the proposed lead compound. In each table, clearly indicate the compound ID/name of the molecular entity from which the data were generated. In the first group of tables, provide the structure of the chemical lead compound for a new molecular entity or provide the composition for a new biological entity.

**Proposals submitted without chemical structures or compositions will not be accepted.**

Populate the tables with any current physical property data, *in vitro* and *in vivo* efficacy data, PK data, and Chemistry, Manufacturing and Controls data on the proposed lead compound. If there are no data generated for a particular property, leave the data cell empty or enter N/A if not available for your proposal (e.g., if the agent is a biologic). Do not delete any cells in the tables. If there are relevant data specific to your proposal, but no rows in the existing tables are designated to accommodate those data, add rows and clearly label what type of data are included. (NOTE: Populated data tables are part of the Appendix and not page limited. Because the fillable data tables are attached to the proposal template, the tables should be uploaded with the research description as a single PDF, not uploaded in the Appendix as a separate file.)

#### **2. Timelines and Milestones (Required)**

Outline a potential timeline for the conduct of studies needed to file the IND application. The timeline should highlight potential milestones and go/no-go decision points. A timeline chart is acceptable. Following approval of a collaboration proposal, NCATS staff may modify the timeline, milestones and go/no-go decision points based on expert scientific opinion, regulatory guidance and contract availability.

#### **3. References (Required)**

Provide a list of no more than 15 references relating directly to the proposal. Upload any key reference papers/manuscripts to ensure that NIH staff and external experts have access to the critical data you wish to cite. Compile and upload all reference documents as a single PDF, if permitted by individual file-size limits in [proposalCENTRAL](#).

#### **4. Regulatory Communications (Required, if applicable)**

If applicable, provide formal meeting minutes or informal written communications from interactions with the FDA.

### 5. *Key Method and Models (Required)*

To help assess the current state of the project and the strength of the data package, investigators must provide a detailed description of any key *in vitro* and/or *in vivo* assay methods including dose/concentration ranges and positive and negative controls.

### 6. *Study Report Summaries (Optional)*

If applicable, provide a one-page summary of results from any relevant pre-clinical study reports (e.g., non-GLP dose range finding toxicology). Full study reports should **not** be uploaded. Summaries may be provided from the study reports to provide greater detail regarding any conclusions drawn in the proposal.

### 7. *Intellectual Property Information (Required)*

List any patents issued or pending with respect to either the agent or to any non-commercially available technology/material required for the development of the agent. In the event that a proposal requires the use of non-commercially available technology/equipment that is patented by a third party, the investigator must provide documentation of the patent holder's approval of NCATS' use of said technology.

### 8. *Key Investigator Biosketches (Required)*

All key investigator (i.e., all investigators intellectually involved in the project) biosketches should follow the new [NIH General Biographical Sketch Format](#). In the list of publications, highlight any publications that are directly related to the proposed project by preceding them with a double asterisk (\*\*). The lead principal investigator (point of contact) should provide additional contact information.

### **Selection Process**

Proposals to BrIDGs are initially assessed by NCATS staff for scope and internal resource availability. NCATS then will solicit feedback on select proposals from NIH staff in relevant Institutes and Centers and external drug development experts. The feedback will be used to measure enthusiasm for the proposed science, competitiveness within the disease research area and feasibility of development. Feedback will be obtained in the following areas:

- Strength of current data package
- Target and therapeutic validation
- Potential to reach first-in-human clinical trials
- Medical impact relative to current standard of care

NCATS will also assess the strength of the investigator's IP estate in its consideration of the project. Although details of NIH and external expert deliberations are kept confidential by the BrIDGs program, investigators will receive written communication regarding the proposal's final outcome.

Following the scientific assessment, select proposals will be further evaluated through due diligence and face-to-face meetings with potential collaborators, during which additional supporting data will be requested by BrIDGs. Portfolio balance and resource availability will also affect final decisions.

### **Post-Request Communications**

NCATS staff will inform investigators of the status of their proposal as soon as is feasible. During the selection process, additional (just-in-time) data may not be submitted. Twelve months after a proposal is deferred or declined, investigators may be given one opportunity to provide new data in support of the proposal. Significant changes to a proposal's scientific direction or available data may require submission of a fully revised proposal document.

### **Project Implementation**

After a project is approved, BrIDGs staff work with principal investigators to develop a plan for the conduct of proposed studies. Development proceeds sequentially in most cases, and the start of one

segment of the project (e.g., toxicology) depends on satisfactory completion of preceding segments (e.g., formulation).

Once a plan is in place, NCATS executes a collaboration agreement with the collaborating organization to document the terms under which data and material will be transferred. BrIDGs staff then assigns studies to existing contractors or competitively solicits new contracts as needed. Selected contractors perform tasks under the direction of BrIDGs scientists. Interim study updates are provided to investigators monthly. Meetings or conference calls may be held, as needed, with the principal investigator to discuss the direction of the project. Final study reports are provided, as they become available, in a format ready for an IND application. Although formal regulatory affairs assistance is not provided by BrIDGs, NCATS staff may provide advice on pre-IND interactions with FDA and filing of the IND.

The principal investigator or a third-party collaborator is responsible for filing the IND application. After the IND is cleared, BrIDGs will release to the principal investigator any clinical trial material that has been made. Investigators are responsible for securing resources for the funding and conduct of clinical trials enabled by BrIDGs data and material.

### **Project Delays and Discontinuations**

BrIDGs is neither a complete drug development program nor an unconditional commitment to develop a particular therapeutic agent for the clinic. The collaboration may encounter difficulties that are scientific (e.g., unwieldy synthesis, poor safety margin, unanticipated toxicity) or administrative (e.g., cuts to funding or contract capacity). Insurmountable difficulties encountered during the development process may force the delay or discontinuation of an entire project.