

## Application Instructions

### **Bridging Interventional Development Gaps (BrIDGs) Program** *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 preclinical 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.

NIH established the [BrIDGs program](#) (formerly known as NIH-Rapid Access to Interventional Development) to make available, on a competitive basis, certain critical resources needed for the development of therapeutic agents. The program's goal is to generate the data and clinical material that investigators need to file an Investigational New Drug (IND) application with the Food and Drug Administration (FDA).

BrIDGs is not a grant program. Researchers with successful projects gain access to government contract resources and assistance with establishing a product development plan. Project funding is provided by the [NIH Common Fund](#) and collaborating NIH Institutes and Centers. The total number of awards depends on the number of applications received, their relative scientific merit and the availability of NIH

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.

funds. Approved BrIDGs projects are completed using the contract resources of NCATS, the National Cancer Institute and the National Heart, Lung and Blood Institute.

Application receipt dates will be posted on the program website when available.

### **Available Services**

Potential therapies for any disease or disorder may be submitted. Applications are accepted for the development of the following therapeutic agents:

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

Available services include:

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

### **Program Scope**

All proposed agents should have demonstrated pharmacological activity in an appropriate in vivo disease model via the intended clinical route of administration. 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. Researchers interested in these resources should consider the Molecular Libraries Program, the Therapeutics for Rare and Neglected Diseases program, or consult with extramural program staff at the appropriate NIH Institute or Center to discuss other funding options.

Manufacture of gene vectors is limited to non-Good Manufacturing Practices (GMP) and GMP-grade adeno-associated virus and lentivirus vectors.

In general, manufacture of clinical trial material will be limited to supplies for Phase I trials.

Formulation, PK and toxicology studies in support of Phase II or later trials (including carcinogenicity and reproductive toxicity studies) are not available.

Regulatory affairs support is not offered by BrIDGs. Applicants must identify other resources for preparing their IND.

Funding for clinical trials of any phase is not available.

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

### **Eligibility**

BrIDGs is intended for use by academic institutions, not-for-profit organizations and Small Business Innovation Research (SBIR)-eligible businesses. View the [SBIR-eligibility criteria](#). Foreign academic and nonprofit institutions may apply to BrIDGs. Foreign businesses are not eligible.

### **Confidentiality**

The review and evaluation process is kept confidential by BrIDGs. Information provided to BrIDGs is considered confidential, and all reviewers will sign conflict of interest and confidentiality agreements before accessing applications.

### **Material Transfer**

The output of BrIDGs program activities will be made fully 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 applicant under the terms of a non-negotiable material transfer agreement.

### **Intellectual Property**

It is expected that the originating investigator institution or a collaborating partner will have acquired or be in the process of acquiring appropriate intellectual property protection prior to applying to the program. All intellectual property relevant to the project should be fully described in the application.

As noted previously, most BrIDGs studies will be completed by NIH contractors. Normally, the NIH will not acquire intellectual property rights to inventions made by its staff under the BrIDGs program. NIH contractors, under the Bayh-Dole Act, may elect to retain rights for a contribution they make that rises to the level of invention. However, some contractors, as a term of their funding agreements, have agreed to offer a first option to the originating investigator institution for license negotiation. Certain other contractors or subcontractors may be subject to a Determination of Exceptional Circumstances through which their rights in subject inventions may be assigned to the originating investigator institution.

### ***Application Information***

The BrIDGs application process involves three steps.

The first step is to register with the proposal management website, [proposalCENTRAL](#). Registration in response to this solicitation includes providing a project summary/abstract. The abstract must summarize the proposed activity in a way suitable for public dissemination. The text should describe the therapeutic agent, the disease, the need for improved therapies, and the request for services to BrIDGs. 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, confidential information, or trade secrets in the description. If the application is funded, the abstract may be posted publicly on the BrIDGs website.

After registration, the second step in the process is to schedule a mandatory pre-application call with the BrIDGs program. The purpose of the call is to assess applicant eligibility and orient applicants to the non-traditional application and approval process.

Once eligibility for the program has been confirmed, the final step in the process is to submit an application via proposalCENTRAL. The BrIDGs application 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. (NOTE: The data collection tables provided in Appendix 1 will not count against the 5-page limit.) The description should explain the rationale behind 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 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 in the following areas:

#### **Chemistry**

- Medicinal chemistry optimization performed to date, including identified issues with the proposed molecule
- Acquisition of bulk substance (GMP and non-GMP) and availability of protocols for scale-up production and analytical methods
- Development of suitable formulations
- Production and stability assurance of dosage forms

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

- Evaluation of PK and pharmacodynamics (PD), including oral 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 schedule
- Toxicology studies in rodents and non-rodents, including IND-directed toxicology, with correlative pharmacology and histopathology

#### **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 accepted by 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 tasks that are proposed for completion by BRIDGs contractors. If the investigator or a collaborator intends to conduct tasks that may impact research supported by the program (e.g., the investigator will provide the drug material to the NIH for use in BRIDGs-supported studies), then the investigator should indicate how those tasks will be conducted and funded.

State all current and applied-for sources of support for the project. This includes a summary of the status of past, planned or ongoing negotiations with companies related to licensure or future development of the product. Include information on any peer-reviewed grants or grant applications pertaining to the project.

The applicant should indicate how BrIDGs support would complement, not duplicate, other sources of support. For projects close to clinical application, 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.

### **Justification**

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 approved, and why organizations (biotechnology companies, venture capital firms, pharmaceutical companies) are presently unwilling to fund or develop this project as it currently stands.

### **Timeline and Milestones**

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 acceptance of a project, NIH staff may modify the timeline, milestones and go/no-go decisions points based on review recommendations and contract availability.

### **Required Appendices**

The following appendices are required (except for Key Methods and Models) and are not page limited.

1. **Data Tables:** Tables are provided in the application package to facilitate data collection on the proposed lead compound. In each table, clearly indicate the 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. Populate the tables with any current physical property data, *in vitro* and *in vivo* efficacy data, and PK 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 applicable to your application (e.g., if the agent is a biologic). Do not delete any cells in the tables. If there are relevant data specific to your application, but no rows in the existing tables are designated to accommodate those data, add rows and indicate clearly in the ID column what type of data are included. (NOTE: Although the populated tables are part of the Appendix and not page limited, the fillable table is attached to the research description template. Therefore, the tables should be uploaded with the research description PDF, not the Appendix PDF).
2. **References:** Provide a reference list and upload no more than 15 reference papers/manuscripts from the list as PDF files.
3. **Key Methods and Models:** To help assess the current state of the project and the strength of the data package applicants may provide a detailed description of any key *in vitro* and/or *in vivo* assay methods.
4. **Intellectual Property Information:** 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 an application requires the use of non-commercially available technology/equipment that is patented by a third party, the applicant must provide documentation of the patent holder's approval of the applicant's use of said technology.
5. **Key Investigators Biosketch:** All key investigator (i.e., all investigators intellectually involved in the project) biosketches should follow the [NIH standard 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.

### **Evaluation Process**

Applications to the BrIDGs program are evaluated by an external technical evaluation panel (TEP) consisting of experts in drug development. Applications will be evaluated according to the following criteria:

- Strength of current data package (40 percent)

- Target and therapeutic validation (30 percent)
- Feasibility to reach first-in-human clinical trials (20 percent)
- Medical impact relative to current standard of care (10 percent)

The TEP will also consider the strength of the applicant's intellectual property estate in its evaluation of the project.

Following the TEP evaluation, the top applications will be discussed with NIH staff in relevant Institutes and Centers to assess the potential for synergy and overlap. Due diligence and face-to-face meetings with applicants may be scheduled to gather additional information prior to a final decision. Decisions will be impacted by a final evaluation of program balance, workload distribution and resource availability.

### ***Resubmission Instructions***

Applicants may resubmit their application to BrIDGs one time. The resubmission should include an introduction of up to two pages that explains how the application has been modified and responds to the comments from the scientific reviews. Within the application, changes to the original document should be underlined, italicized or bold-faced. If the changes to the application are so extensive that the majority of the text would be highlighted, then please explain this in the introduction. Otherwise, the research description and appendices should follow the same guidelines as an original application. Resubmissions may only be submitted on published receipt dates.

### ***Project Implementation Summary***

After a project is approved, BrIDGs staff works 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) may depend on satisfactory completion of preceding segments (e.g., formulation).

Once a plan is in place, BrIDGs staff members assign studies to existing contractors, or competitively solicit 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 Investigational New Drug (IND) application. Although formal regulatory affairs assistance is not provided by BrIDGs, our staff can provide advice on filing the IND and participate in pre-IND meetings, if desired.

The principal investigator or a 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.