Critical Path Institute’s Translational Therapeutics Accelerator

FUNDING OPPORTUNITY FOR PROTEIN-BASED THERAPEUTICS DISCOVERY AND DEVELOPMENT

Guidance for Applicants

BioBRIDGe

- Biologics
- Bridging
- Research and Innovation in Drug Development
- Grants

BRIDGING THE DRUG DEVELOPMENT VALLEY OF DEATH

c-path.org/trxa
Introduction

Critical Path Institute's (C-Path) Translational Therapeutics Accelerator (TRxA) is proud to announce the 2024 global Request for Proposals for its Biologics-focused Bridging Research and Innovation in Drug Development Grants (BioBRIDGe). These BioBRIDGe awards are designed to support academic researchers in traversing the drug development valley of death by funding and defining optimal strategies for advancing new, cutting-edge protein-based therapeutics (PBTs) from the lab to patients.

The following elements of this document will assist interested applicants in learning more about TRxA BioBRIDGe awards and understanding what is required to apply for funding and support through this unique therapeutics accelerator program.

- About C-Path and TRxA
- Types of Projects Eligible for BioBRIDGe awards
- The Application Process and Award Notifications
- Pre-Submission Considerations and Consultations
- Scientific Review Process and Review Criteria

About C-Path and TRxA

C-Path is a nonprofit that leads collaborations to accelerate drug development and advance better treatments for people worldwide. As a neutral convener of patient groups, academia, pharmaceutical companies and regulatory agencies, C-Path brings a breadth of scientific and drug development planning not available in other drug accelerator programs. TRxA is uniquely positioned to leverage the expertise available through C-Path’s >20 disease-based consortia, as well as regulatory expertise and project management, to empower your program and your institution to succeed.

TRxA operates as a global therapeutics accelerator that provides funding to academic researchers, as well as:

- Tactical and strategic drug discovery and development expertise, including regulatory science considerations.
- Resources and hands on guidance, working closely with researchers to develop comprehensive data packages for potential drug candidates, a key to garnering interest from biotechnology and pharmaceutical companies to invest in clinical trials.
- Engagement of contract research organizations (CROs) to perform critical discovery phase experiments and/or validate academic studies.
Types of Projects Eligible for BioBRIDGe Awards

Projects eligible for TRxA BioBRIDGe awards include PBTs for the following indications: Rare and orphan diseases, neurodegenerative disease, and pediatrics. Agents must use any of the protein-based platforms below:

- Peptides or proteins
- Regular, bivalent or trivalent antibodies
- Antibody-drug conjugates

BioBRIDGe Award Entry Criteria:

- The mechanism of action of the protein-based therapeutic (PBT) is known.
- One or more PBT have been sufficiently profiled so that the parameters still to be optimized can be quantitatively specified.
- A well-defined candidate progression pathway with established success criteria is in place.
- In vitro pharmacology assays (biochemical and cell-based potency and selectivity) are available in either the applicant’s or collaborator’s laboratories and have been demonstrated to be suitable to drive the characterization and optimization of the PBT.
- There is a strategy for in vivo pharmacodynamic characterization to assess target engagement and efficacy of the PBT, utilizing clinically relevant outcome measures such as biochemical, anatomical and/or functional metrics.
- A defined target product profile (TPP) is in place.
- Small scale manufacturing of PBTs has been demonstrated in either the applicant’s or collaborator’s laboratories and effective purification techniques to reduce contaminants are in place. cGMP manufacturing is feasible and potential manufacturing and scale-up hurdles are addressed in the application.
- A strategy is available to reduce off-target toxicity and the immunogenic potential while maintaining the bioactivity of the PBT molecule.
- The project team is multidisciplinary, and includes members with expertise around the target biology, the platform on which the PBT is based, as well as clinical practice.
- The PBT is patent eligible and unlikely to be blocked by any intellectual property constraints.

At the conclusion of a BioBRIDGe award, success would include the following:

BioBRIDGe Award Success Criteria:

- Optimized PBT
- Activity by the planned route of administration with exposure levels for activity being achievable based on ADME properties
- Characterized in vitro pharmacology properties
- Characterized ADME properties (in vitro and rodent in vivo)
- Demonstrated in vivo pharmacology in pharmacodynamic model
- Toxicity mechanisms are understood and derisked in the development strategy

Cell and gene therapy applications, oligonucleotides, and medical devices are not eligible at this time. Drug repurposing approaches also are not eligible during this funding cycle.

TRxA has no geographical restrictions for grantees, although applicants must be faculty members at a university or non-profit research institution. Intellectual property (IP) remains solely the property of the PI’s Institution.

Ownership rights to the program must reside at a university or not-for-profit research institution. An option or agreement to an exclusive license cannot be in place at the time of funding.

TRxA offers funding up to $250,000 (for up to 12 months) for PBT translational projects. Entry criteria for BioBRIDGe awards are provided below.
The Application Process and Award Notifications

STEP 1

The principal investigator (or co-PIs) will submit a non-confidential pre-proposal that will be reviewed by C-Path’s scientific experts and TRxA’s Programmatic Review Board (PRB), which has broad expertise in drug discovery and development. Details about elements required in pre-proposals are provided in Exhibit A. Applicants are also encouraged to review the sample pre-proposal here (while this sample is for a small molecule project, it illustrates the type of information being requested).

After review, TRxA will invite selected projects to the next step in the process. Due to volume, no formal reviewer feedback will be provided to applicants at this stage, although the TRxA team will make an effort to convey any particular items of interest or concern that were brought up during the PRB’s discussions.

Prior to submission of the pre-proposal, the TRxA team is available to communicate with PIs via email (TRxA@c-path.org) to answer any questions about pre-proposal requirements, the award process, or to seek feedback on how to optimize your submission.

To start building your pre-proposal, click here for access to TRxA’s grant portal. You will be asked to set up a username and password before starting the pre-proposal application. If you encounter any technical issues with the portal, please reference the Portal User’s Guide or email us at TRxA@c-path.org.

The deadline for submitting a pre-proposal through the portal is Thursday, June 27, 2024 by midnight in the time zone in which you are located.

Notifications about whether applicants have been invited to submit a full proposal will be issued the week of August 12, 2024.
STEP 2

Selected applicants will be invited to enter into a confidentiality agreement (CDA) with C-Path before submission of a full proposal. The TRxA team is available to communicate with PIs via email (TRxA@c-path.org) to answer any questions about full proposal requirements or to seek feedback on how to optimize your submission.

Required content for full proposals is provided in Exhibit B. Full proposals will also be submitted through TRxA's grant portal. There may be overlap in questions from the pre-proposal to the full proposal; it is sufficient to repeat information already supplied as the external scientific advisors will not have access to your pre-proposal submission. You can also view our example full proposal for additional insights into what is being requested (while this sample is for a small molecule project, it illustrates the type of information being requested).

The deadline for submitting a full proposal through the portal is Thursday September 26, 2024 by midnight in the time zone in which you are located.

Pre-submission Considerations and Consultations

If not done so at the pre-proposal stage, before submitting a full proposal it is required that you coordinate with your university's tech transfer and/or grants and contracts office in advance of your submission(s) to:

1. Make them aware that you have been invited to submit a full proposal,
2. Provide an opportunity for review of the TRxA award agreement template to ensure the terms would, in principle, be acceptable and,
3. Request a letter of support, which will be needed at the time of full proposal submission.

You will note that the award agreement includes TRxA operational policies and procedures, which are also provided in this document as Exhibit C.

Once again, during this process, the TRxA team is available to communicate via email (TRxA@c-path.org) to answer any questions about proposal requirements, the award process, or to seek feedback on how to optimize your submission.

Scientific Review Process and Review Criteria

Proposals will be reviewed by at least three external scientific advisors and scored for novelty, scientific and technical merit, as well as commercialization potential. A list of these scientific advisors can be found here. TRxA will select up to three proposals to fund, based on results of the reviews and requested funds, as well as programmatic fit. Award notifications will be issued the week of December 16, 2024.

All proposals will be evaluated based on the following criteria:
The project addresses an unmet medical need: The novel PBT should address a significant unmet need and, once approved, will offer a new or significantly improved medical solution for patients.

Novelty: The target, mechanism, or mode of action should have sufficient novelty to be differentiating from approaches already in the marketplace or in the pipeline of biotech and pharmaceutical industries.

Commercial viability: Assuming the project is successful, is there potential to generate interest from industry partners or venture capital groups to further develop the project, based around market positioning and potential, as well as intellectual property (IP) status? Of note, it is expected that broad international protection of composition of matter IP has been or can be obtained.

Sound scientific rationale for the target: The project should be based upon sound scientific evidence, such as data generated by the PI or peer-reviewed scientific publications, for example around the validity of the target and the approach. Liabilities for either the target or the PBT have been identified and are being addressed in the project plan.

Well-structured, quality project plan: The project should be designed to facilitate meaningful outcomes to support the next stage in the PBT development process. Timelines should be realistic, with achievable deliverables clearly articulated. Risk and mitigation strategies should have been identified. Potential clinical approaches have been identified, along with needed biomarkers and endpoints.

Likelihood of success: What is the likelihood that the project will reach its key inflection point, based on the project plan, available resources, and the investigative team? The investigators should be well positioned to successfully implement the research plan, especially when working in collaboration with the TRxA team, collaborators and associated CROs. The resources needed to conduct activities should be in place to achieve the proposed deliverables.

Budget justification: The proposed timeline and budget should be appropriate and realistic. Scheduling of CRO work product should fit within the period of funding.

Overall enthusiasm: Taking the aspects above into account, what is the overall enthusiasm for the proposed project?
Pre-proposal applications will be submitted through TRxA’s grant portal. It is recommended that pre-proposals be created as a Word document, then cut and pasted into appropriate fields in the online application. Character counts will be enforced. The portal can only accept plain text format. It is recommended that bulleted lists, charts and tables not be used (except in the optional one-page attachment for question #13) as they will adversely affect how the portal counts characters. Also, if cut and pasting content from another document, be sure to check that it is not in rich text format.

A detailed budget is not required for the pre-proposal application, but in answering question #18 please keep in mind that IDC for TRxA awards is limited to 10%, and costs for CROs or consultants are not IDC eligible.

1. **Project title**

2. **Names, contact information, and brief background** *(1000 characters maximum)* of principal investigator(s) that highlights expertise available to the proposed project.

3. Names and contact information for co-investigators within or outside your institution, as well as a brief explanation *(1000 characters maximum)* about the reason for the collaboration and the expertise of those listed.

4. **Name and email of Technology Transfer Office Representative**

5. **Name and email of Award Notification Recipient**

6. **Total funding being requested** *(in USD)*

7. **Please provide a non-confidential lay project abstract.** This non-confidential information may be shared with external reviewers and potential co-funders *(2200 characters maximum)*.

8. **What is the therapeutic indication and the target population of this new drug product** *(375 characters maximum)*?

9. **What is the biological target and/or pathway?** Provide the evidence that links this target to the proposed disease indication *(1500 characters maximum)*.

10. **Briefly discuss available treatments (if any), their limitations, and how the proposed project would provide an advantage over these alternative therapeutic approaches.** *(1500 characters maximum)*.

11. **How does this project address an unmet medical need** *(450 characters maximum)*?
12. **Describe the novelty of the project's approach.** If there are marketed products available for the stated indication, or if similar research is being done in this area by competitors, what differentiates this project \( (1000 \text{ characters maximum}) \)?

13. **What scientific rationale is in place that manipulation of this target results in amelioration of disease** \( (1600 \text{ characters maximum}) \)? Please provide figures as appropriate; figures must be readable as printed on a single 8.5" x 11" page at normal 100% scale, so please ensure proper resolution. If appropriate, upload this optional one page with up to four (4) figures to illustrate scientific concepts and findings.

14. **Is there a validated biomarker or clinical assessment available that can be used in human trials and/or preclinical animal experiments that is reasonably likely to predict clinical outcome?** If yes, please describe \( (1500 \text{ characters maximum}) \).

15. **Are there any predictable safety issues that need to be considered in light of the target, anticipated dosing regimen and/or any liabilities of the therapeutic?** Is there a plan for preliminarily evaluating toxicity \( (1000 \text{ characters maximum}) \)?

16. **What is the status of any IP associated with this project and this candidate series?** Provide patent or application numbers if published \( (1500 \text{ characters maximum}) \).

17. **What are the next steps needed to drive the project towards IND and/or commercial interest of potential licensing partners?** How will the production and reproducibility of production of the candidate be optimized or evaluated? Discuss feasibility of production and reproducibility of production of the candidate. Describe how each parameter (potency, selectivity, stability etc.) will be optimized \( (1500 \text{ characters maximum}) \)?

18. **List and describe activities to be performed with the funding requested, in light of the needed next steps mentioned above.** Per activity, indicate availability of assays/technology needed to evaluate compounds, location of the work to be performed (at your institution, a collaborator's laboratory, or a CRO), anticipated timeline and funds needed to complete the work package \( (3300 \text{ characters maximum}) \).

19. **If applicable, provide a list of funding already secured related to the project that would complement TRxA support (e.g., grants, institutional funds).**

20. **References**

21. **List of Abbreviations**

File uploads: One attachment, saved as Scientific_Rationale.pdf
EXHIBIT B
Required Elements of Full Proposal

I. Applicant Information and Requested Grant Amount
□ Project Title (255 characters maximum)
□ Requested amount of funding
□ Name and address of institution
□ PI name and contact details
□ Names and contact information of co-investigators
□ Name of Technology Transfer Office representative. Please attached a Letter of Support from your TTO; save attachment as “LetterofSupport.pdf.”

II. Project Background
Provide an overview of the project and the potential achievable results. The logic underlying the scientific hypothesis should be clearly described, along with a clear explanation of why the proposed work is an efficient and effective way to support the hypothesis. Provide a definition of research specific abbreviations, acronyms, or symbols embedded once throughout the text.

1. **Therapeutic indication and target population.** Describe the therapeutic indication and target population (255 characters maximum). In addition, attach a maximum 3-page target product profile (letter size), save attachment as “TPP.pdf”

2. **Biological Target and/or Pathway (255 characters maximum)**

3. List relevant amino acid sequence of the lead protein based therapeutic (PBT) (In the case of Antibody-Drug Conjugate (ADC) or complex PBTs, an optional 1-page attachment (letter size) can be used to show the linker and payload structure; save attachment as “Structure.pdf”)

4. **Non-Confidential Lay Project Summary (1500 characters maximum)**

5. **How does this project address an unmet medical need? (750 characters maximum)**

6. **What scientific rationale, e.g. genetic evidence, target expression or natural history data, would suggest that manipulation of this target will result in amelioration of disease? (5000 characters maximum and optional 1 page attachment (letter size) with legible figures, save attachment as “Scientific_Rationale.pdf”)

7. **Competitive Landscape. Describe the novelty of the project's approach.** If there are marketed products available for the stated indication, or if similar research is being done in this area by competitors, what differentiates this project? Also, describe how the proposed project would provide an advantage over existing approaches. (3300 characters maximum and optional 1 page attachment (letter size); save attachment as "Competitive_Landscape.pdf")
8. **Biomarkers and Clinical Endpoints?** Describe biomarker(s) or clinical assessment that has been validated for use as a surrogate endpoint that is reasonably likely to predict clinical benefit in human clinical trials and the theoretical or empirical basis for their potential utility. Markers may reference levels of analytes in fluids/samples, radiologically measured parameters, event time frames, or any other objectively measured values used to reach a single interpretation. Specify the aspect of the marker that is measured and the form in which it is used for biological interpretation. *(1600 characters maximum)*

9. **Are there any predictable safety issues or known on-/off-targets associated risks that need to be considered, anticipated dosing regimen and/or any liabilities of the protein based therapeutic(s)?** Describe mitigation strategies if applicable. *(3300 characters and optional 1 page attachment (letter size) with legible figures and figure legends if required, save attachment as "Risks.pdf")*

10. **Describe the activities to be performed to drive the protein based therapeutic towards IND and/or commercial interest.** Provide a detailed description of each biochemical and/or cellular assay, tiered 'go' and 'no-go' decision points/values, choice and rationale of animal models, study design, where each experiment will be performed (i.e. investigator's lab or CRO), methods, and analyses in sufficient detail for assessment of the application. *(6000 characters and optional 2-page attachment, save attachment as "Key_Activities.pdf")*

11. **Describe the strategy to reduce the immunogenic potential while maintaining the bioactivity of the protein based therapeutic(s).** *(1650 characters and optional 1 page attachment, save attachment as "Immunogenicity_Strategy.pdf")*

12. **Replication of key experiment(s).** Reproducibility is key for garnering interest of future investors or licensees; if not done already, please describe which key experiment should be carried out or repeated by a neutral third party to increase the confidence of the robustness of your observations. Please allow for the cost of this work and suggest a CRO to conduct this experiment in the submitted budget. *(1000 characters maximum)*

13. **Provide a Gantt chart of expected project plan covering period of the funding.** Required 1 page attachment (letter size) with legible figures, save attachment as "Gantt.pdf"

14. **Provide a statement, if applicable, explaining how the study conforms to appropriate ethical regulations and guidelines regarding the use of animals in research.** *(750 characters maximum)*

15. **Project Team.** Provide a brief background of each PI and co-PI's expertise as related to this proposal. *(1500 characters)*

16. **Budget.** A detailed budget should be included with the full proposal using the template provided in the portal. Save attachment as "Budget.xls."

17. **Abbreviations**

18. **References**
The following describes policies and procedures that inform TRxA grant operations with respect to, among others, decision making, publications, grant and patent applications and the adjudication process(es); recognizing that the formal legal agreement is the ultimate governing document.

**Scientific decision making and planning of experiments**

Scientific direction of the project is governed by the university's Principal Investigator(s) (PI(s)) together with TRxA personnel (Executive Director and the Director of Drug Discovery and Development). This project team will decide on the order of experiments, based on the team members' expertise and input from external consultants, as appropriate. The team will also define target values for the lead PBT(s) and define go/no-go decision-making points in the project. TRxA reserves the right to either stop funding the project if progress has not been sufficiently made, or, alternatively, increase the amount of funding available for the project if warranted.

**Intellectual property protection and publication of results**

**Decision making around protection of IP**

Care should be taken to not jeopardize the intellectual property (IP) being developed, with support from TRxA, by publishing prior to appropriate protection being in place. Such protection should be sufficient to garner and maintain the interest of biotech and pharma for potential licensing of the IP (ideally worldwide protection, or at minimum the US and EU). The project team will try to achieve consensus on the best IP strategy. However, since IP is owned by the academic institution, their respective tech transfer and/or licensing office is ultimately responsible for making these patent protection decisions. TRxA reserves the right to stop funding the project if protection is not adequate for ultimate commercialization efforts.

**Protection of IP vs publication**

TRxA recognizes the need for publishing in the academic environment for promotion and tenure considerations. With that said, it is requested that adequate efforts are made to delay publication if the project team deems this in the best interest of the project's future licensing opportunities and thus the ability to bring the new medical product towards patient care. Options should be explored to avoid using graduate students or other trainees on the project, who are especially vulnerable to the need to publish to finalize their training. Instead, it is recommended that professional technicians be utilized to execute the work, should publication restrictions be anticipated. With respect to the PI's performance metrics, it should be explored to what extent patent applications can be counted towards promotion and tenure decisions, to further support the delay of publication while not negatively impacting the PI's career development.

**Timing of publication**

Patent applications become public 18 months after the priority date. Therefore, should the project team deem it in the best interest of the commercial prospects of the project to postpone publication, this can only be delayed to a maximum of 15 months after the priority date. This allows the remaining 3 months for manuscript submission, review and potential revisions, to allow simultaneous publication of the patent application with the manuscript, and not give potential competitors more lead time than necessary.
Notification of publication and recognition language

Plans for submission and publication of manuscripts will be tracked in the monthly project team meetings while the project is actively being supported by TRxA. Should manuscript submission and/or publication happen post active TRxA funding, TRxA will need to be notified of publications during follow up reporting, which will be at minimum on an annual basis.

In publications, to recognize TRxA support, please include the following language: "This publication was supported by Critical Path Institute's Translational Therapeutics Accelerator (TRxA)."

Commercialization

The goal of TRxA's support is to improve the likelihood of commercialization of academic drug discovery projects, whether through licensing with an established industry partner, or through venture-backed company formation. The responsibility and decision making for these commercialization efforts ultimately lie with the university’s tech transfer office (TTO) and/or licensing office, with TRxA only serving in an advisory role.

Conflict Resolution

It is anticipated that most differences of opinion on scientific direction, IP protection, or timing of publication can be resolved within the project team by building consensus, keeping in mind the ultimate goal of getting new therapies to patients. Neutral, external consultants can be engaged to provide additional expert advice, to complement the project team's experience. These consultants can be engaged by any party associated with the funded project. However, should consensus be elusive to achieve, the issue can be escalated to an adjudicating committee, composed of leadership from the university and Critical Path Institute. The project team will agree on the final composition of this body and could include individuals such as the Dean of the PI's School or the Vice President of Research at the university, the head of the TTO, the Chief Science Officer of Critical Path Institute and a representative of the Frederick Gardner Cottrell Foundation, which funds TRxA; external consultants could also be included. It is recommended to have a small, odd number of individuals comprising this committee, such as a minimum of three or a maximum of five individuals.

Reporting

The project team will meet monthly via Zoom, Microsoft Teams or a similar platform, to provide a status update and ensure alignment on next steps for the coming weeks. TRxA will provide a template agenda for these meetings to streamline information sharing. Expenditure reports shall be included in monthly project team meetings.

A written report is expected at the 6-month mark; this will be reviewed by TRxA's Scientific Advisory Committee, who will provide feedback on progress and direction. This report is expected to contain both technical and financial information.

A final report will be expected within 60 days of the end of the grant period. Similar to the 6-month report, this submission is expected to contain both technical and financial information. The Scientific Advisory Committee will once again review this report and also provide a recommendation to TRxA's Programmatic Review Board (PRB) for continuation of funding beyond the initial grant period. The PRB will make the final decision on the opportunity to continue funding, depending on progress but also availability of funds in the TRxA portfolio. Exact requirements and process for continuation of funding will be shared towards the end of the project period.

Templates will be provided for all required reports.