### Critical Path Institute’s Translational Therapeutics Accelerator (TRxA)

**FUNDING OPPORTUNITY FOR DRUG DISCOVERY AND DEVELOPMENT**

*Call for Proposals and Guidance for Applicants*

Critical Path Institute’s (C-Path) Translational Therapeutics Accelerator (TRxA) is a global drug discovery support program that leverages C-Path’s proficiency in translational and regulatory science to bridge the drug development “valley of death.” TRxA accomplishes this by providing academic researchers with funding and guidance to define optimal strategies to advance cutting-edge new therapeutics from the lab to clinical trials and, ultimately, patient care.

**APPLICATION PROCESS**

**Step 1**

The principal investigator (or co-PIs) submits a non-confidential pre-proposal to be reviewed by TRxA’s Programmatic Review Board (PRB), which has broad expertise in drug discovery and development. TRxA will select which projects are invited for 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 concern that were brought up during the PRB’s discussions.

It is recommended that PIs coordinate with their university’s tech transfer and/or grants and contracts office in advance of the submission to 1) make them aware of plans to submit a pre-proposal and 2) provide an opportunity for review of the TRxA award agreement template to ensure this would, in principle, be acceptable.

Prior to submission of the pre-proposal, the TRxA team is available to meet with PIs via teleconference to answer any questions about pre-proposal requirements or the award process. These 30-minute consults are available on a first come, first served basis until **March 31, 2023** and can be requested via email to TRxA@c-path.org.

The deadline for submitting a pre-proposal form is **2 PM US ET on April 17, 2023**.

**Step 2**

Selected applicants will be invited to enter into a non-disclosure or confidentiality agreement (NDA or CDA) with C-Path, after which the applicant will upload the chemical structure of the lead molecule(s), and/or any other pertinent confidential information, to a secure website. The TRxA team along with experienced medicinal chemists will review the submitted structures to further select which applications move to Stage 3, where applicants are invited to submit a full proposal.

**Step 3**

PIs who are invited to submit a full proposal will be notified via email by **July 17, 2023**. The deadline for full proposals is **September 15, 2023**. Optional pre-submission consultations with the TRxA team will be available for PIs to answer questions and optimize the proposal and related materials.

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 six proposals to fund, based on results of the reviews and requested funds as well as programmatic fit. Award notifications will be issued by **November 17, 2023**.

<table>
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<tr>
<th>Open call for proposals</th>
<th>APRIL 17</th>
<th>Pre-proposals due</th>
<th>JUNE 2</th>
<th>NDAs initiated</th>
<th>JUNE 30</th>
<th>PIs upload chemical structures</th>
<th>JULY 17</th>
<th>Invitations for full proposals</th>
<th>SEPTEMBER 15</th>
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Projects eligible for TRxA funding include lead optimization and IND-enabling studies, using small molecule approaches. Biologicals, including peptides or antibodies, cell and gene therapy applications and medical devices are not eligible at this time. Natural products or drug repurposing approaches are also not eligible during this funding cycle. Although projects in all therapeutic areas are welcome to apply, initial preference will be given to small molecule approaches in C-Path’s areas of concentration listed below.

TRxA AWARDS

TRxA offers funding and support for three (3) types of translational projects, each with specific entry and success criteria.

**Stage 1**

**Entry criteria**
- Project is in early lead optimization
- Tractable drug leads from multiple chemical series have been identified (demonstration of optimizable structure-activity relationships [SAR])
- Established *in vitro* pharmacology assays (biochemical and cell-based potency and selectivity)
- Established *in vivo* pharmacodynamic model

**Success criteria**
- Well defined compound progression pathway with established success criteria
- Optimized leads from multiple series
  - Characterized *in vitro* pharmacology properties including cell-based activity
  - Characterized absorption, distribution, metabolism and excretion (ADME) properties (*in vitro* and rodent *in vivo*)
  - Demonstrated *in vivo* pharmacology in pharmacodynamic model
- Established *in vivo* efficacy model

**Stage 2**

**Entry criteria**
- Well defined compound progression pathway with established success criteria
- Optimized leads from multiple series
  - Characterized *in vitro* pharmacology properties including cell-based activity
  - Characterized absorption, distribution, metabolism and excretion (ADME) properties (*in vitro* and rodent *in vivo*)
  - Demonstrated *in vivo* pharmacology in pharmacodynamic model
- Established *in vivo* efficacy model

**Success criteria**
- Defined target product profile (TPP) and vetted regulatory plan to achieve the TPP
- Optimized molecule meeting candidate selection success criteria
  - Characterized *in vitro* and *in vivo* pharmacology including demonstrated efficacy in an *in vivo* efficacy model
  - Characterized ADME properties (*in vitro* and rodent/non-rodent *in vivo*)
  - Characterized toxicology properties (*in vitro* and rodent/non-rodent *in vivo*)
  - Defined non-clinical formulation
- Defined active pharmaceutical ingredient (API) scale up and characterization plan

**Stage 3**

**Entry criteria**
- Defined active pharmaceutical ingredient (API) scale up and characterization plan

**Success criteria**
- Defined target product profile (TPP) and vetted regulatory plan to achieve the TPP
- Optimized molecule meeting candidate selection success criteria
  - Characterized *in vitro* and *in vivo* pharmacology including demonstrated efficacy in an *in vivo* efficacy model
  - Characterized ADME properties (*in vitro* and rodent/non-rodent *in vivo*)
  - Characterized toxicology properties (*in vitro* and rodent/non-rodent *in vivo*)
  - Defined non-clinical formulation
- Defined active pharmaceutical ingredient (API) scale up and characterization plan

Applicants must confer with the TRxA team prior to submission of a Stage 3 proposal! Unsolicited Stage 3 proposals will not be considered for funding.
Entry criteria

- Defined target product profile (TPP) and vetted regulatory plan to achieve the TPP
- Optimized molecule meeting candidate selection success criteria
  - Characterized in vitro and in vivo pharmacology including demonstrated efficacy in an in vivo efficacy model
  - Characterized ADME properties (in vitro and rodent/non-rodent in vivo)
  - Characterized toxicology properties (in vitro and rodent/non-rodent in vivo)
  - Defined non-clinical formulation
- Defined active pharmaceutical ingredient (API) scale up and characterization plan

Success criteria

- Adherence to the TPP and regulatory plan
- Well characterized molecule with complete toxicology package to enable first in human study (FIH)
  - General toxicology
  - Safety pharmacology
  - Genetic toxicology
- Optimized good manufacturing practices (GMP) API scale up strategy

Funds awarded through TRxA are provided specifically for the purpose of carrying out direct research studies for the project as documented in the approved research plan (either at the institution or through a CRO). Indirect costs are limited to 10%.

Review criteria

Pre-proposals must be completed in their entirety to be reviewed by TRxA's Programmatic Review Board. All applications will be evaluated based on the following criteria:

1. **The project addresses an unmet medical need**: the novel drug product needs to address a significant unmet need and, once moved into the clinic, will offer a new or significantly improved medical solution for patients.

2. **Novelty**: the target or approach to the target needs to have sufficient novelty to be a differentiating from approaches already in the marketplace or in the pipeline of biotech and the pharmaceutical industry.

3. **Commercial viability**: There is potential for industry partners or venture capital groups to be interested in further development of the project, based around market positioning and potential, as well as intellectual property (IP) status. Of note, it is expected that international protection of composition of matter IP has been or can be obtained.

4. **Sound scientific rationale for the target**: The project should be based around sound scientific evidence, such as data generated by the PI or peer-reviewed scientific publications, for example around the validity of the target.

5. **Well-structured, quality project plan**: The project should be designed to facilitate meaningful outcomes to support the next stage in the drug development pipeline.

6. **PI qualifications**: The project team should be well positioned to successfully implement the research plan, especially when working in collaboration with the TRxA team and associated CROs.

CONTACT INFORMATION:

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ABOUT C-PATH

Critical Path Institute (C-Path) is an independent, nonprofit organization established in 2005 as a public and private partnership. C-Path’s mission is to catalyze the development of new approaches that advance medical innovation and regulatory science, accelerating the path to a healthier world. An international leader in forming collaborations, C-Path has established numerous global consortia that currently include more than 1,600 scientists from government and regulatory agencies, academia, patient organizations, disease foundations, and hundreds of pharmaceutical and biotech companies. C-Path U.S. is headquartered in Tucson, Arizona, C-Path in Europe is headquartered in Amsterdam, Netherlands and C-Path Ltd, operates from Dublin, Ireland with additional staff in multiple other locations. For more information, visit c-path.org.