CRITICAL PATH INSTITUTE

BRIDGING THE DRUG DEVELOPMENT VALLEY OF DEATH

c-path.org/trxa

BRIDGe

Bridging Research and Innovation in Drug Development Grants

FUNDING OPPORTUNITY FOR DRUG DISCOVERY AND DEVELOPMENT

Guidance for Pre-Proposals

Introduction

Critical Path Institute's (C-Path) Translational Therapeutics Accelerator (TRxA) is pleased to announce the 2026 global Request for Proposals (RFP) for its Bridging Research and Innovation in Drug Development Grants (BRIDGe) program.

The BRIDGe program is designed to assist academic investigators in overcoming the well-known drug development "*valley of death*". Through targeted funding and strategic guidance, BRIDGe enables investigators to define and implement effective pathways for advancing promising therapeutic candidates from the laboratory toward clinical evaluation.

In addition to its annual BRIDGe awards accepting applications in the areas of pediatrics, rare and orphan diseases, and brain health, C-Path is proud to partner with the PKD Foundation to offer a special funding track supporting projects focused on polycystic kidney disease. This collaborative funding opportunity aims to accelerate the translation of high-impact discoveries into potential therapeutic interventions that address unmet medical needs.

This document provides a comprehensive overview of the TRxA BRIDGe program and serves as a guide for prospective applicants. It outlines the available funding tracks, eligibility criteria, evaluation considerations, and submission requirements to support the preparation of competitive proposals for funding and development assistance through this specialized translational accelerator.

Contents

About C-Path and TRxA

Critical Path Institute (C-Path) is an independent, non-profit organization that leads collaborative initiatives to accelerate the development of new therapeutics and improve treatments for patients worldwide. Serving as a neutral convener, C-Path brings together stakeholders from patient organizations, academia, industry, and global regulatory agencies to advance scientific innovation and streamline drug development. Through its more than 20 disease- and pathway-focused consortia, C-Path provides a unique infrastructure for data sharing, regulatory science, and translational research.

Within this ecosystem, C-Path's Translational Therapeutics Accelerator (TRxA) operates as a global drug accelerator, dedicated to advancing early-stage discoveries toward clinical readiness. TRxA supports academic investigators by providing both funding and expert guidance, leveraging C-Path's extensive network of scientific, regulatory, and drug development expertise to enhance the translational potential of academic innovations.

In addition to direct funding, TRxA offers grantees the following:

- **Strategic and tactical expertise** in drug discovery and development, including considerations in regulatory science and preclinical strategy.
- **Resources and hands-on guidance** to build comprehensive data packages that strengthen the value and attractiveness of therapeutic candidates for partnership with biotechnology or pharmaceutical companies.
- **Support in engagement of contract research organizations (CROs)** to conduct key discovery-phase experiments and validate academic findings, ensuring data robustness and reproducibility.

Through its Bridging Research and Innovation in Drug Development Grants (BRIDGe) program, TRxA partners with investigators to:

- Identify and refine translational strategies that optimize the potential for successful therapeutic advancement.
- Develop and execute milestone-driven plans for preclinical validation and optimization of lead candidates.
- Strengthen the scientific and technical foundations necessary to attract future investment or partnership with biotechnology and pharmaceutical organizations.

By integrating scientific, regulatory, and drug development expertise, TRxA helps ensure that innovative discoveries are positioned for maximum impact — advancing from academic laboratories toward therapies that benefit patients worldwide.

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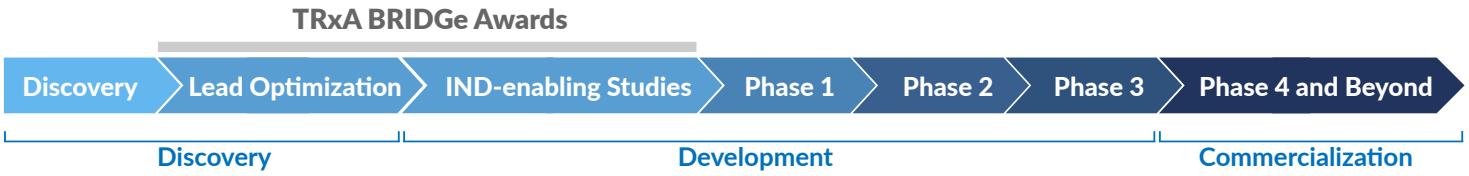
C-Path's mission is to catalyze the development of new approaches that advance medical innovation and regulatory science, accelerating the path to a healthier world.

Eligibility Criteria for TRxA BRIDGe Awards

Projects eligible for TRxA BRIDGe awards include early-stage therapeutic programs focused on lead optimization and IND-enabling studies conducted at academic or non-profit research institutions worldwide.



For the 2026 funding cycle, eligible therapeutic modalities include:

- **Small molecules**
- **Protein-based therapeutics (PBTs)**, including peptides, proteins, conventional, bivalent or trivalent antibodies, peptide-drug conjugates (PDCs), and antibody–drug conjugates (ADCs)
- **In vivo gene-based therapies**

The following areas are not eligible for funding during this cycle: medical devices, drug repurposing approaches, vaccine development, and cell-based therapies.

There are no geographical restrictions for applicants. However, all applicants must hold a faculty appointment or equivalent at a university or non-profit research institution. Ownership of the intellectual property and program assets must reside with the applicant's institution. Projects that are subject to an existing option or exclusive license agreement with a for-profit entity are not eligible for TRxA funding.

Available Funding Tracks

In addition to its annual BRIDGe awards accepting applications in the areas of pediatrics, rare and orphan diseases, and brain health, C-Path is proud to collaborate with the PKD Foundation to expand funding opportunities through a dedicated track focused on polycystic kidney disease. This partnership enables tailored support for high-impact translational projects and further strengthens the bridge between academic innovation and clinical application.

Both tracks benefit from TRxA's integrated accelerator model, which combines financial support with strategic and operational guidance from experts across C-Path's global network of consortia and collaborators.

Polycystic Kidney Disease Foundation (PKDF) Track

The PKD Foundation track supports projects focused on **polycystic kidney disease**, with the goal of accelerating discovery and development efforts in this therapeutic domain. This track provides dedicated funding and access to specialized expertise relevant to the disease area, enabling investigators to advance promising candidates toward clinical readiness.

PKD FOUNDATION
Polycystic kidney disease

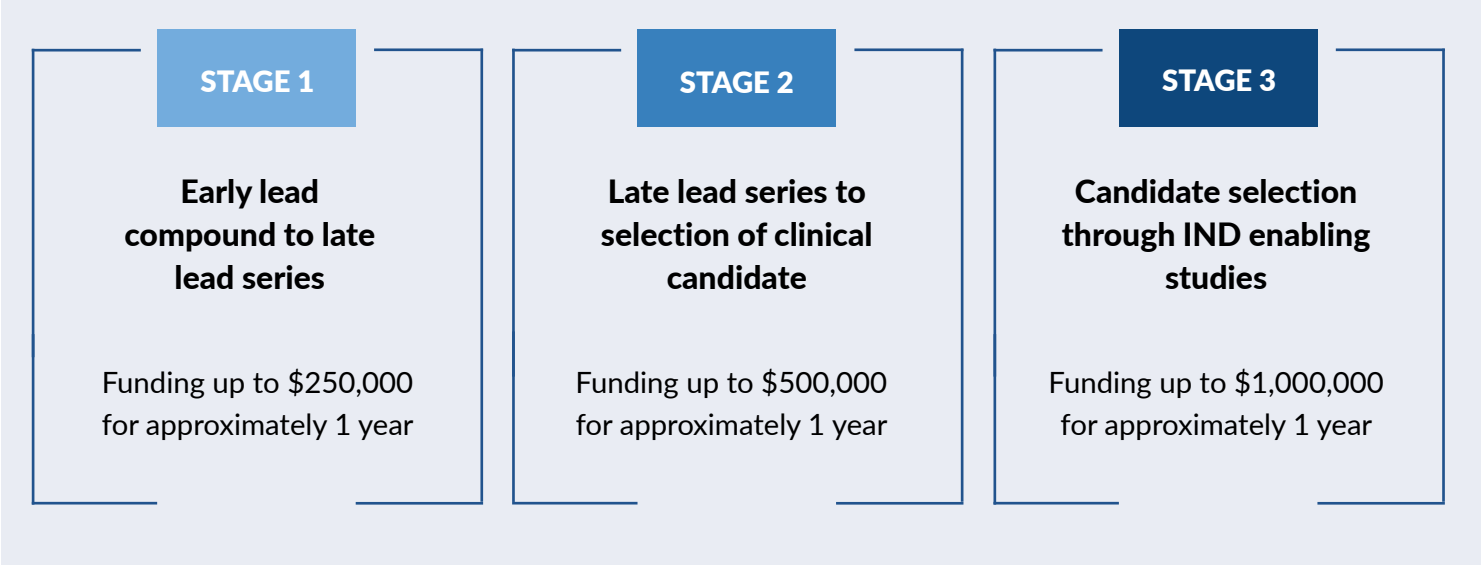
C-Path Track

The C-Path Track is open to proposals across a broad range of therapeutic areas. For the 2026 RFP, applications will be accepted for projects in the following focus areas:

- **Brain health**
- **Pediatrics**
- **Rare and orphan diseases**

Award Structure and Support

C-Path's BRIDGe program provides funding and translational support for three categories of projects, spanning early lead optimization through IND-enabling studies. The available funding levels are illustrated below.



Entry criteria for each stage are detailed in Exhibit A (small molecule projects), Exhibit B (protein-based therapeutics), and Exhibit C (gene-based therapies).

For in vivo gene-based therapy programs, eligible modalities include:

- Gene replacement, including approaches that use target tissues (e.g., liver or kidney) to express missing or mutated proteins
- In vivo gene editing
- Gene silencing
- Delivery platforms with an established clinical track record

The following modalities are not eligible for BRIDGe funding:

- Ex vivo gene editing
- Exosomes as delivery vehicles
- Replication-competent viral vectors (e.g., herpesvirus, poxvirus, VSV)
- Targeting of germline cells

TRxA's award structure is designed to provide not only financial support but also hands-on guidance from experts in drug discovery, development strategy, regulatory science, and project execution, ensuring that funded projects are positioned for maximum translational impact.

The Application Process

The BRIDGe application process consists of three sequential steps, designed to evaluate the scientific merit, translational potential, and feasibility of proposed projects.

Step 1: Pre-Proposal Submission

The Principal Investigator (PI) or Co-Principal Investigators (Co-PIs) must submit a **non-confidential pre-proposal** through the TRxA Grant Portal. Submitted pre-proposals will be reviewed by scientific experts and TRxA's Programmatic Review Board (PRB), which comprises professionals with broad expertise across drug discovery, development, and regulatory science.

Detailed information on required pre-proposal elements is provided in:

- **Exhibit D** – Small Molecules
- **Exhibit E** – Protein-Based Therapeutics (PBTs)
- **Exhibit F** – Gene-Based Therapies

Applicants are encouraged to review a sample pre-proposal prior to submission.

No formal budget is required with submission of a pre-proposal, but applicants must indicate the total funding being requested. When calculating this number, keep in mind that allowable costs include those associated with executing defined project tasks; for example, assay specific lab supplies, animal procurement or core facility services. Not allowed are costs for general laboratory expenses, travel, equipment, tuition, or IP protection.

If salary support is requested, the identified personnel need to be in place at the time of the award so that the work can commence immediately. Salary cannot exceed the current NIH limit ($225,700) and PI contribution is capped at 10% effort. Indirect costs (IDC) are capped at 10%. Costs budgeted for contract research organizations (CROs) and consultants are not eligible for IDC.

It is recommended that applicants coordinate with their university's tech transfer and/or grants and contracts office in advance of the submission to provide an opportunity for review of the TRxA award agreement template to ensure the terms would, in principle, be acceptable.

The deadline for submitting a pre-proposal through the portal is Monday, **March 16, 2026** by midnight in the time zone in which you are located. It is recommended that you set up your username and password at least one week prior to this submission deadline to allow sufficient time for troubleshooting in the event you experience any technical difficulties. Notifications about whether applicants have been invited to advance to Step 2 of the application process will be issued by **May 15, 2026**.

Prior to submission, applicants may contact the TRxA team via email (TRxA@c-path.org) with questions regarding pre-proposal requirements, the award process, or for general feedback to optimize their submission.

Pre-proposals will be evaluated for novelty, scientific and technical merit, and commercialization potential (see *Scientific Review Criteria* section). Based on these evaluations, TRxA will notify applicants whether they have been selected to advance to Step 2 of the application process.

Due to the volume of applications, formal reviewer feedback will not be provided at this stage. However, when possible, the TRxA team will communicate specific points of concern raised during the PRB's discussions.

Applicants can access the TRxA Grant Portal to begin preparing a pre-proposal. A username and password will be required to create an account. For assistance, please refer to the Grant Portal User Guide, or contact TRxA@c-path.org for technical support.

Step 2: Confidential Data Submission

Applicants selected to advance will be invited to enter into a Confidentiality Disclosure Agreement (CDA) with C-Path. Following execution of the CDA, applicants will receive a fillable PDF form to upload confidential project information (e.g., chemical structures) via the TRxA Grant Portal.

This confidential information will be evaluated by TRxA's scientific experts to further assess scientific merit, data robustness, and development feasibility. Based on this review, select applicants will be invited to proceed to Step 3 and submit a full proposal.

During this step applicants will also be asked to complete and upload a brief form detailing current funding sources for the project.

Step 3: Full Proposal Submission

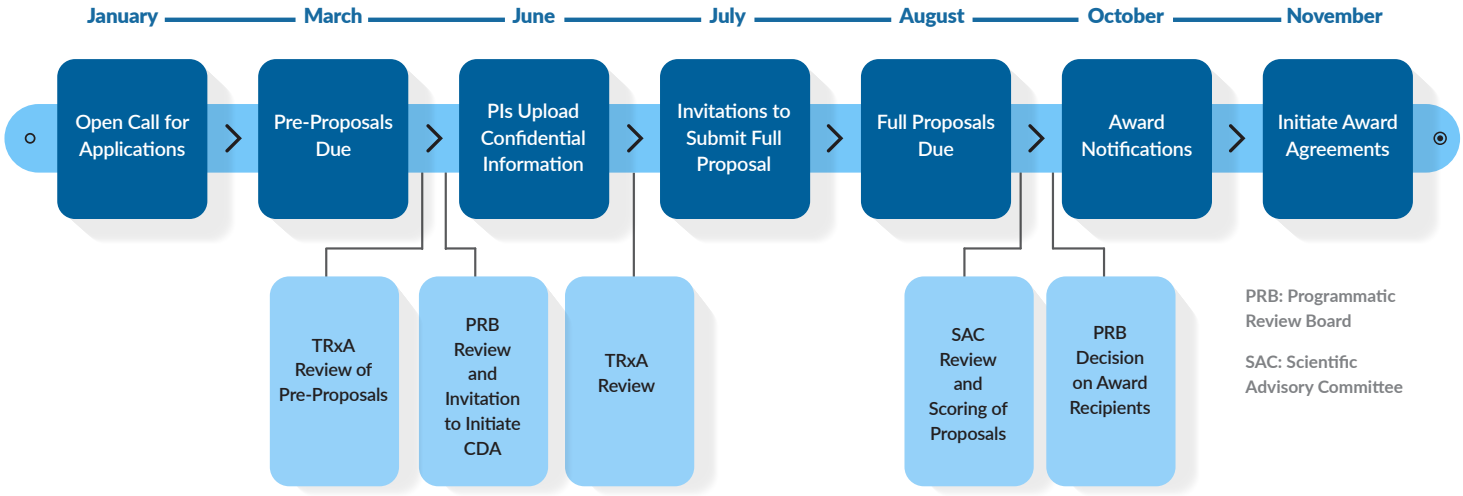
Applicants invited to submit a full proposal will receive formal notification via email by **July 3, 2026**. The **submission deadline** for full proposals is **August 12, 2026**. Detailed requirements for full proposals will be included with the invitation, along with a **sample full proposal** for guidance. Submissions will be made through the TRxA Grant Portal.

Prior to submitting a full proposal, it is required that you coordinate with your university's technology 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. If not done so at the pre-proposal stage, provide an opportunity for review of the TRxA award agreement template to ensure the terms would, in principle, be acceptable (while the TRxA team is available to answer questions about the agreement, please note that negotiation on terms will not commence until receipt of an award notification). You will note that the award agreement includes TRxA's operational policies and procedures, which are also provided in this document as Exhibit G); and,

3. Request a letter of support, which will be needed at the time of full proposal submission.



A detailed budget must be submitted with the full proposal; a template will be provided in the grant portal.

Throughout the 3-step application process, the TRxA team is available via TRxA@c-path.org, to address questions regarding proposal content, submission procedures, or feedback on proposal refinement.

Full proposals will undergo peer review by at least three external scientific advisors (all of whom are bound by confidentiality agreements), who will evaluate and score each application based on novelty, scientific and technical rigor, and commercialization potential. A list of TRxA's external scientific advisors is available here.

Additional details regarding evaluation standards (for pre- and full proposals) are provided in the Scientific Review Criteria section below.

Scientific Review Criteria

All proposals submitted to the BRIDGe program will be evaluated using a structured review process designed to assess the scientific quality, translational potential, and overall feasibility of the proposed research. Each application will be reviewed by qualified experts with relevant domain experience in drug discovery, development, and regulatory science.

Each application will receive an overall impact assessment reflecting the reviewers' judgment of the project's potential to make a meaningful contribution to drug development and patient outcomes.

Pre-proposal applications and full proposals will be evaluated based on the following criteria:

The project addresses an unmet medical need: The novel therapeutic should address a significant unmet need.

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, there should be potential to generate interest from industry partners or venture capital groups to further develop the project, based around market positioning and potential. Key bottlenecks have been addressed and de-risked to achieve full-scale manufacturing without comprising quality of the drug substance. Intellectual property (IP) can be secured within important jurisdictions and there exists the ability to manufacture and market the product without infringing on any others' existing IP rights.

Sound scientific rationale for the target: The project should be based upon sound scientific evidence, such as data supporting the validity of the target and the approach generated by the PI or from peer-reviewed scientific publications. Any predictable liabilities for either the target or the therapeutic 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 drug 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?

Timeline and Award Notification

All submitted proposals will undergo a multi-stage review and selection process, as outlined below. Dates are provided to assist applicants in planning their submissions and coordinating internal institutional approvals.

RFP Announcement	January 20, 2026	Launch of the global Request for Proposals (RFP).
Informational Webinar	January 27, 2026	TRxA-hosted webinar providing an overview of the BRIDGe program, eligibility requirements, and guidance on preparing competitive pre-proposals. Registration details are available on the TRxA website.
Pre-Proposal Submission Deadline	March 16, 2026	Deadline for submission of non-confidential pre-proposals through the TRxA Grant Portal (Step 1).
Notification of Step 2 Eligibility	Week of May 13, 2026	Applicants notified of invitation to submit confidential data packages and notice of support from other funding sources.
Confidential Data Submission Deadline	June 17, 2026	Deadline for submission of confidential data (Step 2).
Notification of Full Proposal Invitation	Week of June 29, 2026	Applicants notified of invitation to submit a full proposal (Step 3).
Full Proposal Submission Deadline	August 12, 2026	Deadline for submission of full proposals through the TRxA Grant Portal.
Final Review and Selection	September–October 2026	Comprehensive scientific review by external experts and the TRxA Programmatic Review Board.
Award Notifications Issued	Week of November 2, 2026	Funding decisions communicated to selected applicants.
Project Start Date	Q1 2027	Initiation of BRIDGe-funded projects upon full execution of project agreement.

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Critical Path Institute (C-Path) is an independent, nonprofit established in 2005 as a public-private partnership, in response to the FDA's Critical Path Initiative. C-Path's mission is to lead collaborations that advance better treatments for people worldwide. Globally recognized as a pioneer in accelerating drug development, C-Path has established numerous international consortia, programs and initiatives that currently include more than 1,600 scientists and representatives from government and regulatory agencies, academia, patient organizations, disease foundations and pharmaceutical and biotech companies. With dedicated team members located throughout the world, C-Path's global headquarters is located in Tucson, Arizona and C-Path's Europe subsidiary is headquartered in Amsterdam, Netherlands. For more information, visit c-path.org.

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Exhibit A

Entry Criteria for Small Molecule Projects

STAGE 1

- The project is in early lead optimization.
- A compound progression pathway with established success criteria has been defined.
- Tractable drug leads from (preferably) multiple chemical series have been identified with a demonstration of optimizable SAR and a range of activity for the lead series, i.e. >10 compounds within 1 log potency of the lead candidate.
- Established *in vitro* pharmacology assays (biochemical and cell-based potency and selectivity) are in place, with the throughput to support lead optimization.
- There is access to an available or conceived in vivo pharmacodynamic model.
- The chemical series is patent eligible and unlikely to be blocked by any intellectual property (IP) constraints.

STAGE 2

- A well-profiled advanced series has been identified and a preclinical candidate will be nominated by the end of the award.
- Optimized candidates from (preferably) multiple series are available, with remaining optimization goals identified.
- A lead series is in place with characterized *in vitro* pharmacology properties, including cell-based activity.
- The lead series has characterized ADME properties (*in vitro* and rodent *in vivo*).
- The lead series has demonstrated *in vivo* target engagement.

STAGE 3

- A clinical candidate has been selected.
- The clinical candidate has characterized *in vitro* and *in vivo* pharmacology, including demonstrated efficacy in an *in vivo* efficacy model.
- The clinical candidate has characterized ADME properties (*in vitro* and rodent/non-rodent *in vivo*) as well as characterized toxicology properties (*in vitro* and rodent/non rodent *in vivo*).
- A non-clinical formulation has been defined.
- A GMP API scale up and characterization plan has been defined.

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Exhibit B

Entry Criteria for PBT Projects

STAGE 1

- The project is in lead optimization.
- A candidate progression pathway with established success criteria has been defined.
- Established *in vitro* pharmacology assays (biochemical and cell-based potency and selectivity) are in place, with the throughput to support lead optimization. These assays have been shown to be suitable to drive the characterization and optimization of the PBT.
- The immunogenicity potential has been assessed and an appropriate derisking strategy is in place.
- The therapeutic has demonstrated *in vivo* target engagement in a pharmacodynamic model.
- The PBT is patent eligible and unlikely to be blocked by any intellectual property (IP) constraints.

STAGE 2

- One or more humanized protein based therapeutic (PBT) molecules have been sufficiently profiled so that the parameters still to be optimized can be quantitatively specified.
- A strategy is available to reduce the immunogenic potential while maintaining the bioactivity of the PBT molecule.
- The therapeutic has demonstrated *in vivo* efficacy, utilizing clinically relevant outcome measures such as biochemical, anatomical and/or functional metrics.
- The therapeutic has characterized ADME properties (*in vitro* and rodent *in vivo*).
- Small scale manufacturing of the candidate is available in either the applicant's or collaborator's laboratories. cGMP manufacturing is feasible and potential manufacturing and scale-up hurdles are addressed in the application.
- The PBT is patent eligible. The delivery, manufacturing or other enabling technologies are not blocked by IP where the acquisition of an exclusive license would be required to practice the invention.

STAGE 3

- A clinical candidate has been identified, which is an optimized, humanized, protein based therapeutic (PBT).
- The clinical candidate has characterized *in vitro* and *in vivo* pharmacology, including demonstrated efficacy in an *in vivo* efficacy model.
- The clinical candidate has characterized ADME properties (*in vitro* and rodent/non-rodent *in vivo*) as well as characterized toxicology properties (*in vitro* and rodent/non rodent *in vivo*)
- A non-clinical formulation has been defined.
- A GMP scale up and characterization plan has been defined.

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Exhibit C

Entry Criteria for Gene-Based Therapies

STAGE 1

- The therapy is intended to treat a pediatric indication, a rare or orphan disease, or is intended to improve brain health.
- The modality is in scope. Eligible therapeutics include in vivo gene-editing, RNA and other oligonucleotide-based modalities, and gene-therapy products
- A draft Target Product Profile (TPP) is complete, demonstrating that the product supports the intended therapeutic use.
- The vector specifically targets somatic cells and is engineered to minimize or eliminate any exposure to germline cells. The vector only targets somatic cells and avoids the germline.
- The intended clinical target tissue and the planned delivery route are well defined.
- For vector-based therapies, the promoter/ enhancer selection achieves desired expression in the target tissue. A developed qPCR titer assay, ELISA for capsid quantification. The applicant has demonstrated functional expression without evidence of cytotoxicity.
- The immunogenicity potential has been assessed and an appropriate de-risking strategy is in place.
- In vivo efficacy has been demonstrated with clinically meaningful endpoints, such as biochemical, anatomical, or functional measures.
- Small-scale manufacturing of the candidate is established within the applicant's or collaborator's laboratories, cGMP manufacturing is considered feasible with scale-up challenges addressed, a relevant potency assay (e.g., in vitro transgene expression) has been developed, and vector stability has been demonstrated in small-scale production.
- Preliminary off-target prediction and in vitro assessment for RNA-targeting modalities has been performed.
- Aggregation, instability, payload size constraints, or delivery limitations — have been assessed.
- The therapy is patent-eligible, and no existing IP related to delivery, manufacturing, or other enabling technologies poses a barrier that would necessitate securing an exclusive license.

STAGE 2

- Production of small-scale preclinical-grade AAV is complete in an external manufacturing facility and potential manufacturing and scale-up hurdles are addressed in the application.
- Biodistribution has been evaluated in a relevant disease or wild-type mouse model.
- The minimum effective dose and plateau of response has been identified. A preliminary maximum feasible dose and dose–response relationship have been established.
- Expression via fluorescence, qPCR, or immunohistochemistry has been assessed.
- Integration or insertion-site analysis (e.g., LAM-PCR, ICE, or NGS-based assays) has been initiated to assess insertion profile and risk.
- Demonstrated functional rescue of phenotype. Efficacy has been benchmarked compared to endogenous gene expression. Proof-of-concept achieved at feasible dose, acceptable local tolerance.
- Preclinical safety program planned including assessment of toxicology, genotoxicity/integration assessment, immunogenicity, on- and off-target expression, reproductive and developmental toxicity if relevant in species that predict human distribution and toxicity.

STAGE 3

- A reproducible scale-up manufacture and batch consistency has been demonstrated.
- Minimal immune activation at clinical dose neutralizing antibodies
- NOAEL established; no systemic toxicity demonstrated in species that predict human distribution and toxicity.
- A GMP scale-up and characterization plan has been defined.
- The therapy is patent eligible. The delivery, manufacturing or other enabling technologies are not blocked by IP where the acquisition of an exclusive license would be required to practice the invention.

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Exhibit D

Pre-Proposal Application for Small Molecule Projects

1. Project title
2. Names, contact information, and brief background (1,000 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 (1,000 characters maximum) about the reason for the collaboration and the expertise of those listed.
4. Name and email of Technology Transfer Office representative
5. Therapeutic area (select from drop down list in grant portal)
6. Type of award being requested (Stage 1, 2 or 3)
7. Please provide a non-confidential project abstract. This non-confidential information may be shared with external reviewers and potential co-funders (2,200 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 (250 characters maximum)?
10. 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 (1,000 characters maximum)?
11. What scientific rationale, in addition to any genetic evidence, is in place that demonstrates manipulation of this target results in amelioration of disease? (2,500 characters maximum)? Include a discussion of the relevance of the chosen animal model to clinical application. 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 appropriate resolution. If appropriate, upload this optional one-page with up to four (4) figures to illustrate scientific concepts and findings.
12. 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. (1,500 characters maximum)
13. 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 compound(s)? (450 characters maximum)
14. What is the status of any IP associated with this project and this compound/compound series? Provide patent or application numbers if published (1,500 characters maximum)
15. What are the next steps needed to drive the project towards IND and/or commercial interest of potential licensing partners (1,500 characters maximum)?
16. 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, throughput and turnaround times, location of the work to be performed (at your institution, a collaborator, or a CRO), anticipated timeline and funds needed to complete the work package. (3,300 characters maximum).
17. If applicable, list funding already secured related to the project that would complement TRxA support (e.g., grants, institutional funds).
18. References
19. List of abbreviations

File uploads: Optional one-page attachment, saved as "scientificrationale.pdf" (see question #11)

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Exhibit E

Pre-Proposal Application for Protein-Based Therapeutics Projects

1. Project title
2. Names, contact information, and brief background (1,000 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 (1,000 characters maximum) about the reason for the collaboration and the expertise of those listed.
4. Name and email of Technology Transfer Office representative
5. Therapeutic area (select from drop down list in grant portal)
6. Type of award being requested (Stage 1, 2 or 3)
7. Please provide a non-confidential project abstract. This non-confidential information may be shared with external reviewers and potential co-funders (2,200 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 (250 characters maximum)?
10. 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 (1,000 characters maximum)?
11. What scientific rationale is in place that demonstrates that manipulation of this target results in amelioration of disease? (2,500 characters maximum)? Include a discussion of the relevance of the chosen animal model to clinical application. 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 appropriate resolution. If appropriate, upload this one page with up to four (4) figures to illustrate scientific concepts and findings.
12. 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. (1,500 characters maximum)
13. 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 and derisking immunogenicity and/or toxicity? (1,000 characters maximum)
14. What is the status of any IP associated with this project and this candidate series? Provide patent or application numbers if published (1,500 characters maximum)
15. What are the next steps needed to drive the project towards IND and/or commercial interest of potential licensing partners, and how will the production and reproducibility of manufacturing of the candidate be optimized or evaluated? Discuss the feasibility, challenges and robustness of the manufacturing. Describe how each parameter (potency, selectivity, stability etc.) will be optimized (2,000 characters maximum)?
16. List and describe activities to be performed with the funding requested, in light of the next steps needed above. Per activity, indicate availability of assays/technology needed to evaluate candidates, throughput and turnaround times, location of the work to be performed (at your institution, a collaborator, or a CRO), anticipated timeline and funds needed to complete the work package. (3,300 characters maximum).
17. If applicable, list of funding already secured related to the project that would complement TRxA support (e.g., grants, institutional funds).
18. References
19. List of abbreviations

File uploads: One optional attachment, saved as scientificrationale.pdf (see question #11)

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Exhibit F

Pre-Proposal Application for Gene-Based Therapy Projects

1. Project title
2. Names, contact information, and brief background (1,000 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 (1,000 characters maximum) about the reason for the collaboration and the expertise of those listed.
4. Name and email of Technology Transfer Office representative
5. Therapeutic area (select from drop down list in grant portal)
6. Type of award being requested (Stage 1, 2 or 3)
7. Please provide a non-confidential project abstract. This non-confidential information may be shared with external reviewers and potential co-funders (2,200 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 (250 characters maximum)?
10. 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 (1,000 characters maximum)?
11. What scientific rationale is in place that demonstrates that manipulation of this target results in amelioration of disease? (2,500 characters maximum)? Include a discussion of the relevance of the chosen animal model to clinical application. 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 appropriate resolution. If appropriate, upload this one page with up to four (4) figures to illustrate scientific concepts and findings.
12. 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. (1,500 characters maximum)
13. Are there any predictable safety issues that need to be considered in light of the target, the vector, anticipated dosing regimen and/or any liabilities of the therapeutic. Is there a plan for preliminarily evaluating and derisking immunogenicity and/or toxicity? (1,000 characters maximum)
14. What is the status of any IP associated with this project and this candidate series? Provide patent or application numbers if published (1,500 characters maximum)
15. What are the next steps needed to drive the project towards IND and/or commercial interest of potential licensing partners. Also discuss the feasibility, challenges and robustness of manufacturing of the therapeutic molecule. Describe how each parameter (potency, selectivity, stability etc.) will be optimized (2,000 characters maximum).
16. List and describe activities to be performed with the funding requested, in light of the next steps needed above. Per activity, indicate availability of assays/technology needed to evaluate candidates, throughput and turnaround times, location of the work to be performed (at your institution, a collaborator, or a CRO), anticipated timeline and funds needed to complete the work package. (3,300 characters maximum).
17. If applicable, list of funding already secured related to the project that would complement TRxA support (e.g., grants, institutional funds).
18. References
19. List of abbreviations

File uploads: One optional attachment, saved as scientificrationale.pdf (see question #11)

CRITICAL PATH INSTITUTE

Exhibit G

TRxA Operational Policies and Procedures

This document 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 molecule(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) and the PKD Foundation."

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 provided quarterly, as well as prior to requesting milestone payments, and shall include a breakdown of expenditures of any sub awardees.

A written report is required at the 6-month mark and should be submitted within 30 days of this date; 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 required within 30 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.