National Institute of Neurological Disorders and Stroke

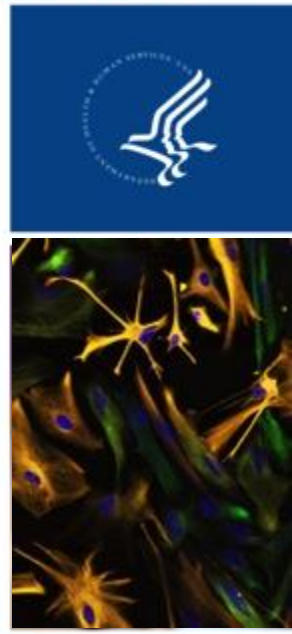
URGenT
Ultra-Rare Gene-based Therapy

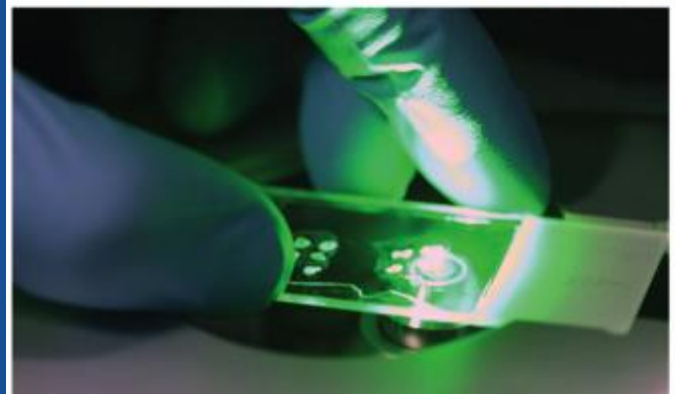
NINDS URGenT Program Webinar

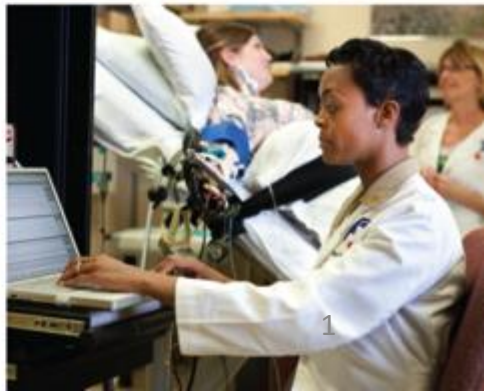
Chris H. Boshoff Ph.D.

April 21, 2022

3:00 – 4:00 PM EST



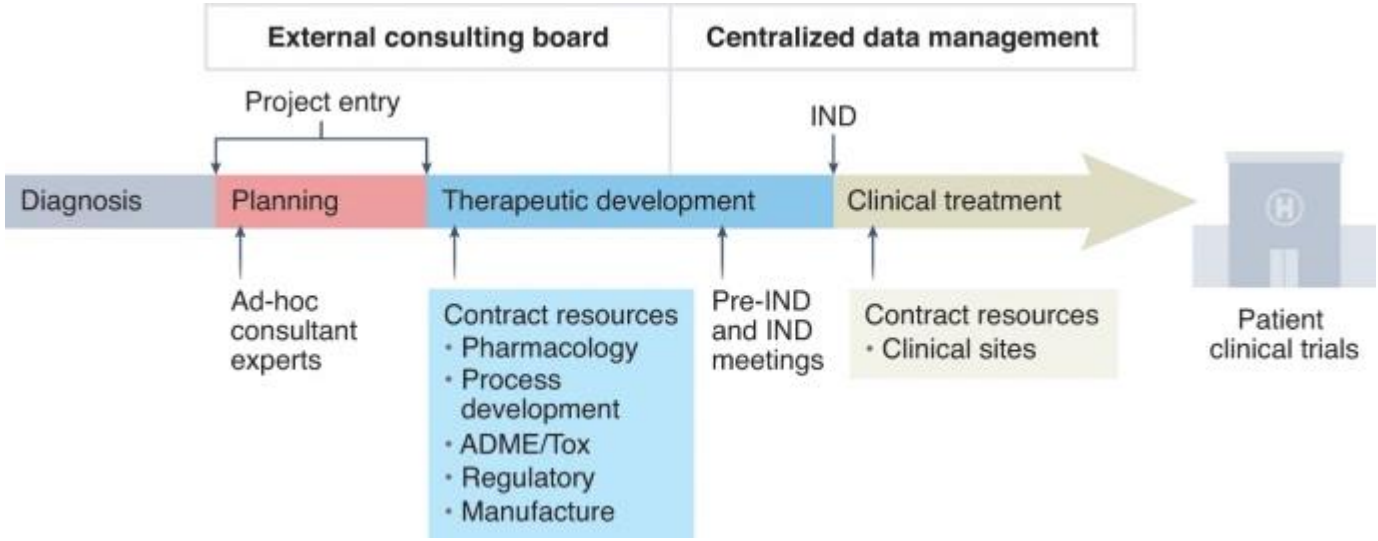




Ultra-Rare Gene Therapy Network

URGenT will provide support for the development of state-of-the-art **gene-based therapies for ultra-rare neurological diseases**

- Phased program with **multiple entry points**
- Funding and resources to advance gene-based therapies **from late-stage nonclinical development into clinical testing**
- Accelerated development timeline - **3 years start to finish**



Correspondence | Published: 04 November 2021

NINDS launches network to develop treatments for ultra-rare neurological diseases

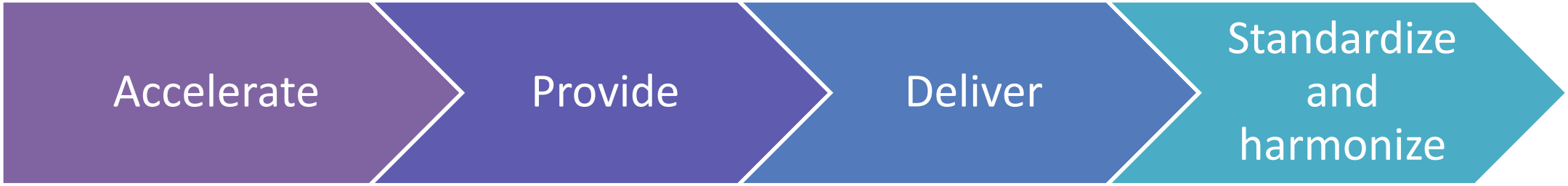
Nina F. Schor, Amir P. Tamiz, Walter J. Koroshetz, NINDS Ultra-Rare Gene-based Therapy (URGenT) Working Group & Ann-Marie Broome

Nature Biotechnology **39**, 1497–1499 (2021) | Cite this article

882 Accesses | **15** Altmetric | Metrics

NINDS URGenT Program Goals

The mission of the network is to provide resources and funding for the scientific community to develop gene-targeted therapies from bench to bedside for ultra-rare diseases



- ✓ Accelerate advancement of discoveries
- ✓ Provide resources and expertise such as appropriate contract partners,
- ✓ Provide external consulting board that will oversee all aspects of the projects.
- ✓ Deliver therapeutics
- ✓ Standardize and harmonize best practices and protocols

Scope

Ultra-rare Disease affect substantially fewer people, less than or equal to 6,000; in the U.S., this equates to as few or fewer than one in 50,000 people

Gene-based or transcript-directed therapeutics include but are not limited to:

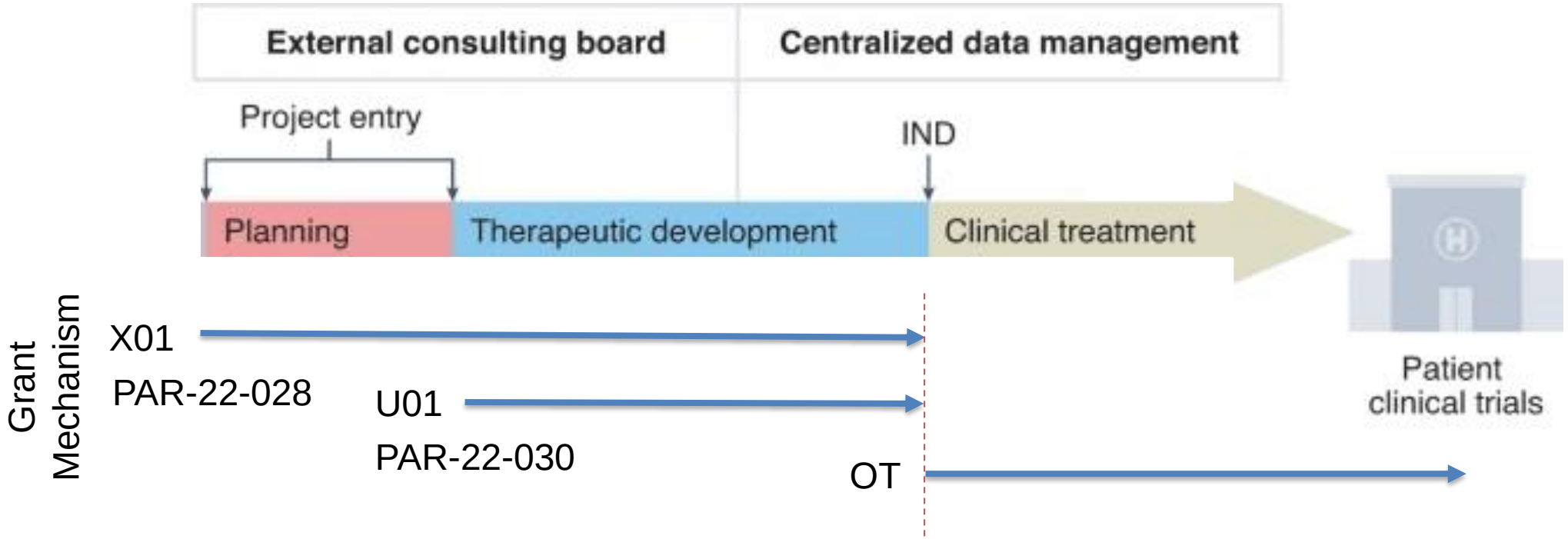
- Oligonucleotide-based approaches
- Viral vector-based approaches
- Genome editing-based approaches
- Other gene-based therapeutic approaches

NINDS URGenT Program : Current Funding Opportunities

Number	Title	Mechanism
PAR-22-028	Ultra-Rare Gene-based Therapy (URGenT) Network Resource Access	X01
PAR-22-030	Translational Efforts to Advance Gene-based Therapies for Ultra-Rare Neurological and Neuromuscular Disorders	U01

X01=Resource Access Program
U01 = Research Project - Cooperative Agreements
*Only **U01** PAR is Clinical Trial Optional*

URGenT Grant Mechanism



PAR-22-028 & PAR-22-030 – Award Mechanisms

Mechanism	Mechanism Name	Length	Milestones	Budget	Intellectual Property
X01	Resource Access Program	Up to 3 years	Yes, determined by investigators, NIH staff and SMEs	Not Applicable; **funds are not awarded** via the X01 mechanism	The awardee institution retains their assignment of intellectual property (IP) rights and gains assignment of IP rights from the URGenT contractors
U01	Research Project - Cooperative Agreements	Up to 3 years	Yes, determined by investigators, NIH staff and SMEs	**Not limited**, but should reflect the needs of the project	The awardee institution retains their assignment of intellectual property (IP) rights and gains assignment of IP rights from the URGenT contractors

Entry Requirements

- The **POC data** establishes the **feasibility** and rationale for candidate use with effective dose range using appropriate assays.
- The Program Director/Principal Investigator (PD/PI**) identified a gene-based or transcript-directed therapeutic clinical candidate** supported by *in vivo* and/or *in vitro* data (efficacy and preliminary safety).
- The PD/PI **has held formal pre-IND discussions**
- The PD/PI **can provide an outline** of the future clinical trial

Supports Late-Stage Nonclinical Development

Applications proposing plans for nonclinical development in parallel with clinical planning activities, including, but not limited to:

- **Manufacturing** (i.e., technology transfer, process development etc. and clinical scale cGMP manufacturing)
- **Qualification and/or validation** of any bioassays for IND-enabling nonclinical and clinical studies
- IND-enabling **efficacy studies** with intended clinical grade product and **safety and toxicology** testing in relevant animal model(s)
- Assessment of off-target affects
- Evaluation utility of **pharmacodynamic/target engagement biomarkers** associated with the therapeutic target or disease
- Completion of all clinical trial planning activities (IRB)
- Preparation and submission of an **IND package**

Cooperative Agreement

Structure

- For each project provided access to the network, the NINDS will assemble a customized **Multi-disciplinary Project Team (MPT)**.
- The MPT will include members of the **Program Director/Principal Investigator's (PD/PI) team** and additional **SME consultants**.
- The MPT will establish **an overall strategy** for the project with milestones, including **a plan and timeline**, and will develop and coordinate activities across different URGenT contract resources.

General Information

Funding Opportunity Announcements

- PAR-22-028 (X01)
- PAR-22-030 (U01)

Next U01 receipt dates in 2022:

- June 9, October 8

Next X01 Applications:

- Rolling applications

URGenT Website

RESEARCH FUNDED BY NINDS

- Clinical Research
- Neuroscience Research
- Translational Research

LATEST UPDATES

NINDS Strategic Plan 2021-2026

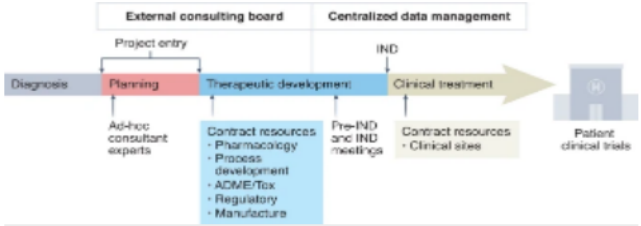
Read more

Ultra-rare Gene-based Therapy (URGenT) Network

The Ultra-rare Gene-based Therapy (URGenT) program will support the development of state-of-the-art gene-based therapies for ultra-rare neurological diseases, which affect as few or fewer than one in fifty thousand people. Altogether, around 7,000 known rare and ultra-rare diseases affect 30 million people in the US. Many are life-threatening and few have FDA-approved treatments. About 45% of rare diseases, including ultra-rare diseases, are neurological disorders, and 90% of rare childhood disorders have major neurological effects. 85% of rare and ultra-rare diseases are single gene disorders, making them excellent candidates for gene therapy. The URGenT program will provide funding and resources to advance gene-based therapies for ultra-rare neurological diseases from late-stage pre-clinical development into first-in-human clinical testing.

The goals of the URGenT program are to:

1. **Accelerate** advancement of discoveries into the clinic.
2. **Provide** resources and expertise not currently available to applicants.
3. **Deliver** therapeutics to patients with ultra-rare neurological diseases.
4. **Standardize** and **harmonize** best practices and protocols for the development of gene-based therapies for ultra-rare diseases.



Overview of the URGenT network - URGenT will support PIs with a lead gene therapy candidate from start-to-finish over a 3-year period. Projects enter before or after the planning stage, during which access to specialized consultants is available as needed. Appropriate contract partners are provided to aid with different stages of therapeutic development (including manufacturing, IND-enabling PK/toxicology studies, and IND submission), and transition to clinical trials. All aspects will be overseen by an external consulting board. Centralized data management ensures facilitative sharing of data, resources and practices with other projects in the network. ADME, absorption, distribution, metabolism and excretion; IND, Investigational New Drug; tox, toxicology.

URGenT Funding Opportunities

PAR-22-030: Translational Efforts to Advance Gene-based Therapies for Ultra-Rare Neurological and Neuromuscular Disorders (U01 - Clinical Trial Optional)

PAR-22-028: Ultra-Rare Gene-based Therapy (URGenT) Network Resource Access (X01, Clinical Trial Not Allowed)

Contact

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Related Funding Announcements

URGenT Funding Opportunities

View All Funding Opportunities

News & Events

URGenT Network Information Session
April 21, 2022 | 3PM EST

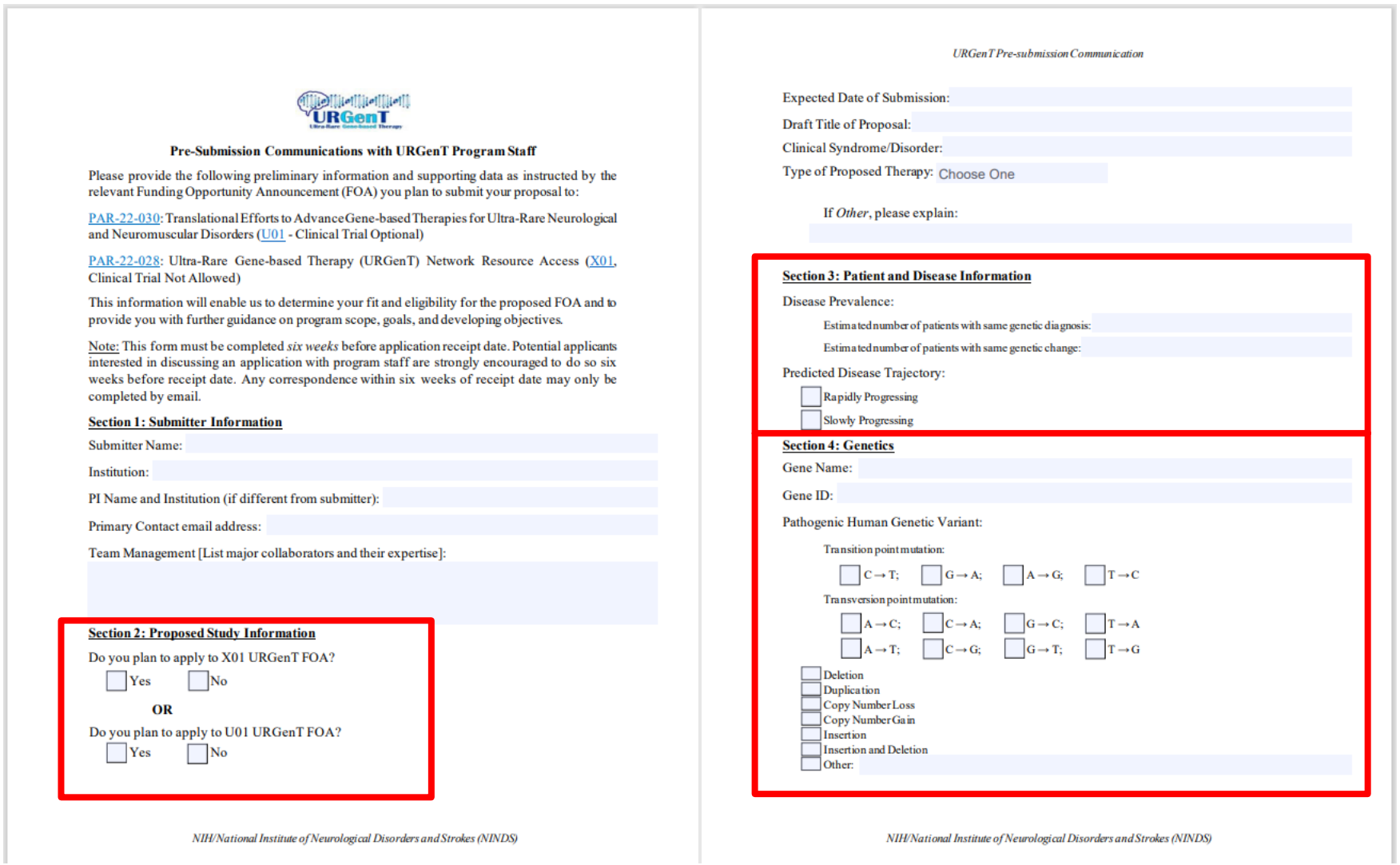
NINDS launches network to develop treatments for ultra-rare neurological diseases
November 4, 2021

Contact information

Future webinars

FOA information

URGenT Pre-application Form



Pre-Submission Communications with URGenT Program Staff

Please provide the following preliminary information and supporting data as instructed by the relevant Funding Opportunity Announcement (FOA) you plan to submit your proposal to:

PAR-22-030: Translational Efforts to Advance Gene-based Therapies for Ultra-Rare Neurological and Neuromuscular Disorders (U01 - Clinical Trial Optional)

PAR-22-028: Ultra-Rare Gene-based Therapy (URGenT) Network Resource Access (X01, Clinical Trial Not Allowed)

This information will enable us to determine your fit and eligibility for the proposed FOA and to provide you with further guidance on program scope, goals, and developing objectives.

Note: This form must be completed *six weeks* before application receipt date. Potential applicants interested in discussing an application with program staff are strongly encouraged to do so six weeks before receipt date. Any correspondence within six weeks of receipt date may only be completed by email.

Section 1: Submitter Information

Submitter Name:

Institution:

PI Name and Institution (if different from submitter):

Primary Contact email address:

Team Management [List major collaborators and their expertise]:

Section 2: Proposed Study Information

Do you plan to apply to X01 URGenT FOA?

☐ Yes ☐ No

OR

Do you plan to apply to U01 URGenT FOA?

☐ Yes ☐ No

NIH/National Institute of Neurological Disorders and Strokes (NINDS)

URGenT Pre-submission Communication

Expected Date of Submission:

Draft Title of Proposal:

Clinical Syndrome/Disorder:

Type of Proposed Therapy: Choose One

If *Other*, please explain:

Section 3: Patient and Disease Information

Disease Prevalence:

Estimated number of patients with same genetic diagnosis:

Estimated number of patients with same genetic change:

Predicted Disease Trajectory:

☐ Rapidly Progressing

☐ Slowly Progressing

Section 4: Genetics

Gene Name:

Gene ID:

Pathogenic Human Genetic Variant:

Transition point mutation:

☐ C → T; ☐ G → A; ☐ A → G; ☐ T → C

Transversion point mutation:

☐ A → C; ☐ C → A; ☐ G → C; ☐ T → A

☐ A → T; ☐ C → G; ☐ G → T; ☐ T → G

☐ Deletion
☐ Duplication
☐ Copy Number Loss
☐ Copy Number Gain
☐ Insertion
☐ Insertion and Deletion
☐ Other:

NIH/National Institute of Neurological Disorders and Strokes (NINDS)

Program Contacts

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QUESTIONS?