Foundation for the National Institutes of Health

Disease Nomination Form
for the
Bespoke Gene Therapy Consortium Clinical Program

The Foundation for the National Institutes of Health (FNIH), in association with various NIH and private-sector partners, is publishing this form to solicit nominations for rare diseases and disorders to be included in the Accelerating Medicines Partnership® (AMP®) Bespoke Gene Therapy Consortium (BGTC). The BGTC clinical program aims to select 5-6 monogenic diseases and disorders that would be suitable for gene therapy using adeno-associated virus (AAV) vectors. The goal of the BGTC clinical program is to streamline the process of AAV gene therapy clinical trials initiation and use the results of the pilot clinical trials to create a more standardized regulatory submission package for use in future AAV clinical efforts. The BGTC is committed to developing a clinical program that includes a diverse patient population across the clinical trial participants, and will strive to select a set of diseases and disorders that collectively represent age, gender, geographical, racial and ethnic diversity.

Submitted diseases and disorders must meet the established definition of a rare disease (i.e., 200,000 patients or fewer in the United States); preference will be given to diseases and disorders with low commercial interest, whether "ultra-rare" or due to other characteristics. Nominations for both pediatric and adult diseases and disorders will be evaluated by the BGTC Steering Committee according to the required and preferred criteria below, and selected nominations will be invited to submit a full Request for Proposals (RFP) application for the opportunity to advance an AAV gene therapy candidate through first-in-human clinical trials. Additional factors will be considered during the RFP review, including clinical trial costs, ability to obtain AAV vector manufacturing, patient diversity, and overall program diversity. Selected RFPs will be connected with industry partners who will produce the GMP vector to be used in IND-enabling (GLP, toxicity, etc.) studies conducted and/or coordinated by the BGTC cores, and, if successful, a human clinical trial conducted at either the NIH Clinical Center or an external site as appropriate.

The BGTC Steering Committee strongly encourages coordination between patient groups and established government, academic, or industry researchers and/or clinicians, in order to provide the most complete information in the nomination form and reduce duplicate nominations for the same disease or disorder. Completed forms should be sent to BGTC@fnih.org with the subject line "Disease Nomination Form" by 11:59PM EST February 18, 2022. Invitations to submit a full RFP are expected to be sent in late March 2022.

Required Criteria

A. Monogenetic disease or disorder with a therapeutically relevant gene target that can be successfully inserted into an AAV vector
B. At least one proof of concept study, either *in vivo* or in an appropriate cellular/organoid model, supporting an AAV gene therapy approach (published or unpublished)
C. One or more disease models (e.g., cellular, organoid, or animal) able to demonstrate transgene functionality, dose finding studies, and conduct safety and efficacy testing
D. At least one validated, clinical meaningful outcome measure with suitability for an AAV gene therapy clinical trial (well-justified biomarkers are eligible), optimally justified by natural history study data and/or prior use in clinical trials
E. Route of administration that has been used in a prior approved IND, and anticipated total patient dose
F. Serious or life-threatening condition, with benefit/risk ratio sufficient to justify AAV exposure
G. Condition affects 200,000 persons in the US or fewer
H. No existing known commercial programs developing a gene therapy for this disease

Preferred Criteria

I. At least one natural history study or non-AAV clinical trial registered worldwide, with sufficient disease progression data to inform future clinical trial design
J. Evidence supporting a favorable safety profile (e.g., overexpression or knock-down safety, prior GLP/toxicity studies)
K. Evidence supporting a favorable therapeutic window for producing a clinically relevant outcome in a patient through delivery of an AAV gene therapy
L. High unmet clinical need (e.g., no treatments or other disease modifying therapies available or under clinical development)
M. Discernable effect on clinical outcome measure in <2 years expected
N. Evidence of viable path to clinical trial recruitment for a first-in-human trial, such as:
    a. Existing contact registry
    b. Existence of one or more relevant patient advocacy group(s)
    c. Interest/support from an established clinical investigator

Disease Information (This section addresses the following required and preferred criteria: F, G, H, L)

1. Specific disease/disorder name and target gene:

2. Prevalence in the US:

3. Briefly describe the patient community demographics (including age, gender, race, ethnicity, geographic distribution and/or other disadvantaged populations):

4. Briefly describe the clinical presentation of the disease/disorder (including estimated patient lifespan, if relevant), and any AAV-gene therapies or other disease modifying therapies available or under clinical development:

Previous R&D Work (This section addresses the following required and preferred criteria: A, B, C, D, I, J)

5. Briefly describe the pre-clinical research history of the disease/disorder (e.g., proof of concept studies, relevant disease models, clinical outcome measures or biomarkers, or other relevant pre-clinical results):

6. Briefly describe the clinical research history of the disease/disorder (e.g., safety studies, prior natural history studies, prior non-AAV clinical trials, or other relevant clinical results):

Clinical Trial Information (This section addresses the following required and preferred criteria: E, K, M, N)

7. What is the expected route of administration and the anticipated total patient dose (vector genomes per kilogram) of an AAV vector?

8. What is the expected therapeutic window (e.g., time from diagnosis, patient age, progression marker) to produce a clinically relevant outcome in a patient through delivery of an AAV gene therapy?

9. Approximately how long would a clinical trial need to follow patients in order to reach a clinically relevant endpoint?

10. Does the disease/disorder have:
    a. An existing contact registry? ☐ Yes (please describe below) ☐ No

    b. An existing/supportive patient advocacy group? ☐ Yes (please describe below) ☐ No

    c. Interest/support from an established clinical investigator and/or a potential clinical trial site? ☐ Yes (please describe below) ☐ No

11. Are there any other factors that would address anticipated challenges to patient recruitment? ☐ Yes (please describe below) ☐ No

Submitter Information

Name:

Organization:

Email:

☐Patient Advocate ☐Clinician ☐Researcher ☐Other

Name:

Organization:

Email:

☐Patient Advocate ☐Clinician ☐Researcher ☐Other

Name:

Organization:

Email:

☐Patient Advocate ☐Clinician ☐Researcher ☐Other

Name:

Organization:

Email:

☐Patient Advocate ☐Clinician ☐Researcher ☐Other

Name:

Organization:

Email:

☐Patient Advocate ☐Clinician ☐Researcher ☐Other