The NINDS Ultra-Rare Gene-based Therapy Network: An URGenT need for ultra-rare neurological diseases

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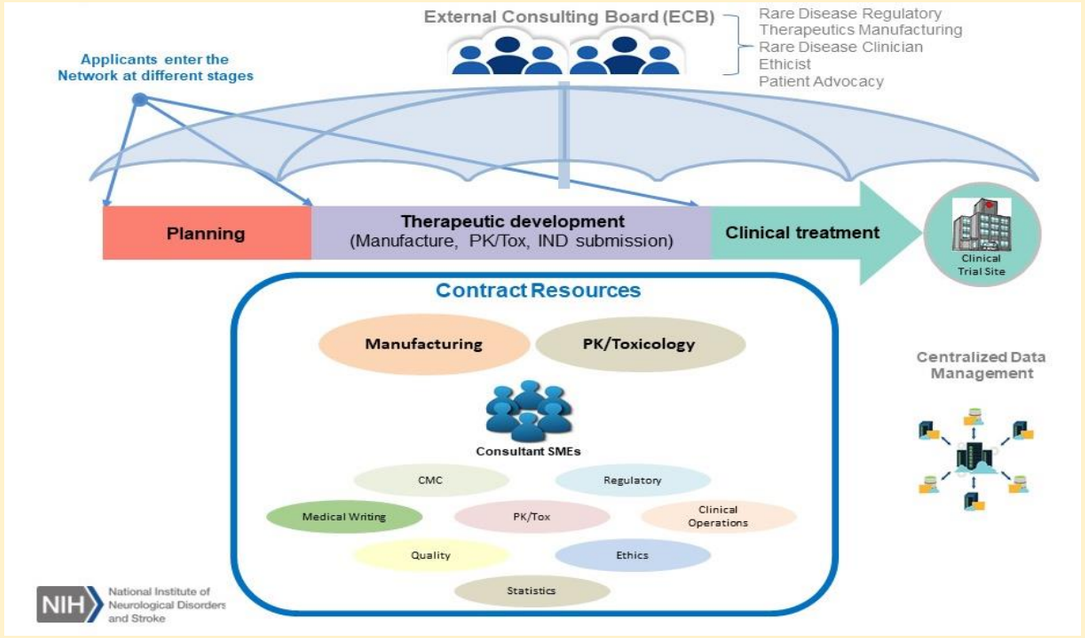
Gene-based therapies, including viral and oligo-based approaches as well as gene editing, have begun to change the medical options and outcomes for patients with rare and ultra-rare genetic disorders. Availability of and access to these therapies is limited by prohibitive costs, risk of failure, challenges in manufacturing, and novel regulatory requirements. Furthermore, institutions differ widely in the resources, expertise, and risk tolerance they can apply to providing patients with such individualized therapies. NINDS has created a mechanism that will enable wider development and deployment of gene-based therapies.

Challenges for Advancement from Early Discovery towards Clinical Trials

- Complex regulatory path
- Raising funds
- Recruiting interest from academic researchers
  - Basic disease mechanisms
  - Experience in preclinical research to clinical trial design
- Access to therapy development experience
- Access to manufacturing and toxicology resources
- Gaining the interest of industry
- Unique statistical considerations
- Other challenges
  - Natural history studies
  - Recruitment of patients



URGenT Network Goals:

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

Successful applicants will have access to the following resources:

- **cGMP manufacturing** of clinical lots of viral-based (e.g., AAVs, lentiviruses), oligo-based (e.g., ASO, siRNA, mRNA) and other biotherapeutics;
- GLP IND-enabling **PK and toxicology** testing;
- **Subject matter expert consultants** (e.g., manufacturing, PK/toxicology, regulatory affairs/operations)

URGenT will provide, on a competitive basis, both grant funding and access to in-kind resources for planning and execution of therapeutic agent optimization, scale up and manufacture, IND-enabling studies, regulatory affairs support including IND preparation and submission, and clinical trial performance. The first requests for applications are anticipated to be issued in 2021.