CAN GRANT CONCEPT CLEARANCE RECORD
FY 2019 RESEARCH INITIATIVE — NCATS
December 2017 Concept #2

CONCEPT TITLE: NCATS Collaborative Rare Disease Platform Vector Gene Therapy Trial

CONCEPT TYPE: Cooperative Agreement

ASSIGNED DISCUSSANTS: Bartek, O'Boyle

OBJECTIVE(S): From a therapeutic standpoint, viral vectors are vehicles to deliver nucleic acids to specific cell types. As such, they are inherently platforms, applicable to the treatment of multiple diseases resulting from abnormalities in the same cell types. However, the current approach to gene therapy clinical trials is still "one disease at a time," which does not maximize the inherent platform capacity of viral vectors. This results in duplication of effort and delay in trial startup.

To address this roadblock, NCATS proposes a novel public-private partnership model for explicitly platform-based gene therapy clinical trials. The approach involves using well-characterized viral vectors as gene delivery vehicles for the treatment of at least three rare genetic diseases that share the same therapeutic target tissue or cell type. To maximize efficiency, therapeutic vectors for all diseases in a platform trial will be produced in the same manufacturing facility and will undergo Investigational New Drug (IND)-enabling (toxicity and biodistribution) studies in parallel, using processes developed by the NCATS Division of Pre-Clinical Innovation (DPI). The diseases chosen for this gene therapy platform trial should be those currently under study within the Rare Diseases Clinical Research Network (RDCRN), to maximize the benefit of natural history data and disease-specific expertise within the program. The NCATS Office of Strategic Alliances (OSA) will play a key role in creating agreements and managing interactions and partnership between NCATS, academia and industry partners.

Specific objectives are to:

1. test a public-private partnership model for platform-based gene therapy clinical trials in rare diseases;
2. expand human gene therapy trials to more patients within the RDCRN;
3. increase the efficiency of trial start up by minimizing redundancies in pre-clinical IND-enabling steps; and
4. enhance collaboration and leveraging of existing resources and expertise across NCATS' Office of Rare Diseases Research/RDCRN, DPI, and OSA.

CAN PROJECT CRITERIA:

- **Collaborative:** Involves three different divisions/offices of NCATS (i.e., ORDR, DPI, OSA), as well as involvement of academic investigators, rare disease patient groups and biotech partners.
- **Discrete and Measurable Outcomes:** Number of rare disease patients from different diseases enrolled in gene therapy trials, time to INDs, increased efficiency of trial start-up process, number of follow-on clinical trials using the same platform.
- **Broad and Significant Impact:** Moving away from "one disease at a time" to platforms for delivering nucleic acid therapeutics across multiple related diseases, based on therapeutic target cell type.
- **Disease Relevance:** Broad applicability to many diseases; the platform approach could target cell types in different organs.

HISTORY: Two human gene therapy drugs have been approved in Europe. Luxturna (voretigene neparvovec-rzyl) was unanimously recommended by a U.S. Food and Drug Administration advisory committee for FDA approval in October 2017 and was approved for marketing by the FDA on Dec. 19, 2017. This is the first viral vector-based gene therapy for a rare disease to be approved in the U.S. Other rare disease gene therapy trials in spinal muscular atrophy, aromatic L-amino acid decarboxylase deficiency, hemophilia, and adenosine deaminase severe combined immunodeficiency have also shown promising clinical results.

On July 18, 2017, NCATS issued a Request for Information (RFI) entitled Opportunities and Challenges for Platform Vector Human Gene Therapy Trials in Rare Diseases (NOT-TR-17-019). The goal of this RFI was to obtain feedback from the community on this topic. Overall, the responses indicated broad enthusiasm for the platform vector approach, as well as indications that such efforts are under consideration currently.

CONCEPT CLEARANCE DATE:
December 15, 2017

COUNCIL RECOMMENDATION:
The CAN Review Board approved as presented.

PROJECT/PROGRAM OFFICERS:
Philip John (P.J.) Brooks, Ph.D.
Program Director
Division of Clinical Innovation
Phone: 301-443-0513
Email: pj.brooks@mail.nih.gov

Nora N. Yang, Ph.D.
Senior Scientist, Therapeutics for Rare and Neglected Diseases, Director, Portfolio Management and Strategic Operations
Division of Pre-Clinical Innovation
Phone: 301-827-0929
Email: nora.yang@nih.gov

Lili Portilla, M.P.A.
Director of Strategic Alliances
Office of Strategic Alliances
Phone: 301-827-7170
Email: portilll@mail.nih.gov