Johns Hopkins Medicine
All Children's Hospital Institutional Biosafety Committee
JHACH IBC Minutes for November 7, 2025
Zoom Meeting

Members Present: Martin Trapecar, Ph.D. (IBC Chair, Medicine – Endocrinology and Metabolism); Neil A Goldenberg, MD, Ph.D. (Pediatrics – Hematology); Stephen C. Dahl, Ph.D., RBP (BSO, Biology); Nasreen Haideri, Ph.D. (Non-affiliated Member); Gary S. Hayward, Ph.D. (IBC Chair, Virology and Gene Therapy); Jane F. Pfeilsticker, M.S., (Non-affiliated Member); Weiying Pan, Ph.D., RBP (Associate BSO, Molecular Aspect of Drug Design and Biology); Nadia Desir, Ph.D., RBP (Associate BSO, High Containment); Alan F. Scott, Ph.D. (Molecular Biology and Genetics); Rui Zhou, Ph.D. (Medicine – Endocrinology and Metabolism); Milton Griggs, BS (Project Manager, Safety Administration)

Members Absent: Jason Villano, D.V.M. (IBC member, Animal Science)

IBC Coordinator: Ms. Tylicia McRae

The Meeting was called to order at 11:03 am.

Announcements:

Dr. Goldenberg disclosed an academic relationship with Dr. Leiding and will abstain from voting on Dr. Leiding's protocol.

Review and Approval of Meeting Minutes:

The minutes of the June 4, 2025 meeting were approved as submitted.

Clinical protocols and Amendments:

Leiding Protocol, GT2511070101 (NIH CIT.: III-C-1), "A Phase 1/2 Open-Label Single-Ascending-Dose Study of EN-374, a Helper-Dependent Adenoviral-Based Gene Therapy, in Patients with X-Linked Chronic Granulomatous Disease"

The objectives of this study are to evaluate the safety and potential efficacy of EN-374 in the treatment of X-Linked Chronic Granulomatous Disease, as well as to determine an appropriate dose for further evaluation. EN-374 consists of two independent helper-dependent adenoviruses designed to genetically modify hematopoietic stem cells (HSCs) to express the wild-type CYBB gene. The study will be conducted in two parts. Part 1 is a single-ascending-dose study in adult participants to determine the dose of EN-374 for dose expansion in Part 2. A maximum of 12 participants will be enrolled in two sequential dose cohorts. Part 2 is a dose-expansion study to evaluate the dose of EN-374 identified in Part 1 in pediatric participants. A maximum of 18

participants will be enrolled in three age cohorts. Part 2 of the study will not start enrollment until all participants in Part 1 of the study have completed three 28-day enrichment cycles with O^6-BG/TMZ.

Participants will be expected to enroll in a separate long-term follow-up study and be followed for approximately 15 years after infusion.

Dr. Trapecar noted that the Investigator's Brochure received was unsigned and labeled as a draft. It did not include detailed information regarding risk descriptions, vector characterization, a nonclinical biodistribution/persistence summary informing reproductive risk, a shedding assessment plan, and precautions. Dr. Trapecar would like to reach out to Dr. Leiding to request the updated Investigator's Brochure, as well as the SOPs for product and waste handling and required training.

The IBC voted for conditional approval pending receipt of the required information described above.

Dr. Leiding subsequently submitted a signed, updated version of the Investigator's Brochure (version 2), which included all required details, a summary addressing the questions, and JHACH pharmacy SOPs covering product and waste handling as well as required training. Dr. Trapecar and Dr. Dahl reviewed the revised submission and confirmed that it complied with the requirements of the Johns Hopkins IBC, institutional policies, and the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

Final IBC approval was granted following receipt and review of the revised submission.

For Approval: 10
Disapproval: 0
Abstain: 1 (Dr. Goldenberg)

Recombinant NDA/Pathogen Research Registrations and Amendments:

No research registrations were presented for IBC consideration.

Review of Incidents:

No incidents were reported at this meeting.

Public Comments:

There were no public comments.

The meeting was adjourned at 1:30 pm.