Johns Hopkins Medicine – Kennedy Krieger Institutional Biosafety Committee
JHM-KKI IBC Minutes for June 16, 2025
Zoom Meeting

Members Present: Gary S. Hayward, Ph.D. (IBC Chair, Virology and Gene Therapy); Weiying Pan, Ph.D., RBP (Associate BSO, Molecular Aspect of Drug Design and Biology); Stephen C. Dahl, Ph.D., RBP (BSO, Biology); Alan F. Scott, Ph.D. (IBC member, Molecular Biology and Genetics); Nadia Desir, Ph.D., RBP (Associate BSO, High Containment); Elizabeth A. Laffan, Ph.D. (Non-affiliated Member, Biology); Ms. Claudia MacAuley, L.A.T. (Non-affiliated Member, Biosafety and High Containment); Djikolngar Maouyo, Ph.D. (Non-affiliated Member, Biology); Viji Sitther, Ph.D. (Non-affiliated Member, Plant Biology); Mr. Daniel Hendrickson, MS, MA (IBC member, Assistant Vice President, Safety, Security, and Environment of Care)

Members Absent: Jason Villano, D.V.M. (IBC member, Animal Science); Brigitte Gaume, Ph.D. (Non-affiliated Member, Biology)

Guests: Ms. Anita Stone (Executive Director, Occupational and Environmental Safety)

IBC Coordinator: Ms. Tylicia McRae

The meeting was called to order at 3:15 pm.

Announcements:

No conflicts of interest were reported by IBC members.

The minutes from the May 19, 2025 meeting were approved as submitted.

Clinical Protocols:

Leung Protocol, GT2506160301 (NIH Cit.: III-C-1), A Phase 1/2, Open-Label, Dose-Escalation Study to Evaluate the Safety, Tolerability, and Biological Activity of EPI-321, an AAVrh74-delivered Epigenetic Editing Therapy in Adult FSHD Patients

The primary objective of this first-in-human clinical trial is to evaluate the safety, tolerability, and biological activity of EPI-321. EPI-321 consists of a recombinant adeno-associated virus vector, serotype rh74 (AAVrh74), designed to deliver genetic material encoding an epigenetic editing system. Up to nine participants between 18 and 75 years of age will be enrolled to evaluate up to two dose levels of EPI-321. The dose for Cohort 1 will be 2.0×10^{13} vg/kg, and the dose for Cohort 2 will be 4.0×10^{13} vg/kg. Patients will receive a one-time treatment of EPI-

321 via slow peripheral venous infusion in an inpatient setting with close monitoring. Enrollment in Cohort 2 will be based on recommendations from an independent safety monitoring committee.

To inhibit the immune response to the AAV-based therapy, patients will receive an oral dose of prophylactic prednisone or an equivalent starting on Day -3 and continuing through Day 60, followed by a gradual taper. Patients will remain inpatient for two days following dosing and must stay within a one-hour drive of the study site for at least two weeks after treatment. The duration of the study is approximately five years, including two months for screening and baseline evaluations.

The medical and pharmacy staff involved in the study will be trained to follow the pharmacy manual for the proper handling of EPI-321, as well as the standard operating procedures (SOPs) for incident management, including spill response, before the trial begins.

The submission complies with the requirements of the Johns Hopkins IBC, institutional policies, and the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

The IBC voted to approve the protocol.

For Approval: 10
Disapproval: 0
Abstain: 0

Smith-Hicks Protocol, GT2506160201 (NIH Cit.: III-C-1), A Phase 1/2, Open-Label Clinical Study to Evaluate Safety, Tolerability, and Efficacy of NGN-401 in Subjects with Rett Syndrome

The primary objective of this protocol is to evaluate the safety and tolerability of NGN-401, administered via a single unilateral intracerebroventricular infusion, in female patients with Rett Syndrome. NGN-401 is a non-replicating, recombinant AAV9 gene therapy that contains a full-length version of the MECP2 gene and is designed to express therapeutic levels of MECP2 protein while avoiding overexpression.

Approximately 14 participants will be enrolled in this first-in-human study. The study includes two dose-escalation cohorts (Cohorts 1 and 2) for patients aged 4 to 10 years, and one cohort for patients aged 11 years and older (Cohort 4). The planned dose-expansion Cohort 3 has been discontinued. Cohorts 1 and 4 will receive a low dose of 1.0×10^{15} vg, while Cohort 2 will receive a high dose of 3.0×10^{15} vg.

Patients in Cohorts 1 and 4 will receive prophylactic corticosteroids starting one day prior to dosing and continuing for 90 days post-dose to reduce the risk of an immune response to the AAV9-based therapy. Patients in Cohort 2 will receive rituximab infusions beginning on Study Day -14, a course of oral sirolimus starting seven days before dosing, and a combination of

prophylactic immunosuppressants initiated one day prior to NGN-401 administration. Sirolimus will be continued for 90 days following treatment.

All patients will be admitted to the pediatric intensive care unit (PICU) and remain inpatient through Day 5 post-dose for monitoring and assessments. Following discharge, patients must remain local to the study site for the first two weeks for frequent study visits and monitoring and stay within a two-hour travel distance of the study center for at least three months.

Patients will be followed closely for five years. The total duration of the study is approximately six years, after which participants are expected to enroll in a 10-year long-term follow-up study.

The medical and pharmacy staff involved in the study have been trained to follow the pharmacy manual for the proper handling of NGN-401, as well as the standard operating procedures (SOPs) for incident management, including spill response.

The submission complies with the requirements of the Johns Hopkins IBC, institutional policies, and the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

The IBC voted to approve the protocol.

For Approval: 10
Disapproval: 0
Abstain: 0

Review of Incidents:

No incidents were reported at this meeting.

Public Comments:

There were no public comments.

The meeting was adjourned at 3:53 pm.