

Institutional Biosafety Committee:

Present: Dr. Steven Albelda, Dr. Julian Baptiste, Dr. Jessica Buchanan, Dr. Sara Cherry, Dorothy Kaplan, Dr. Daniel Kessler, Dr. Andrew Maksymowych, Dr. Maureen O’Leary, Dr. David Pegues, Ms. Jessa Yoos, Ms. Denene Wambach

Absent: Dr. Paul Bates, Dr. Joseph Fraietta

Invited Guests: Ms. Stephanie Adams, Dr. Sarah Capasso, Ms. Marie-Luise Faber, Dr. Tucker Piergallini, Mr. Edwin Siu, Ms. Amanda Wong, Ms. Kimberly Craig, Adriana Fraser

The Institutional Biosafety Committee Meeting was called to order by Dr. Daniel Kessler at **10:00 AM**.

1. IBC Minutes: 11-24-2025

- The IBC reviewed the IBC Minutes.
- All members are in favor of approval as submitted.
- Minutes approved as submitted.

2. Registrations for Review:

SECTION III–C. Experiments Involving Human Gene Transfer that Require IBC & IRB Approval Prior to Initiation:

1. Aleman.....#25-382 C-1

Dr. Tomas S Aleman– NEW HGT Protocol Registration.....**FULL REVIEW**

PROTOCOL TITLE: A Phase 1b/2a, Open Label, Dose Exploration Study to Investigate the Safety and Tolerability of Subretinally Injected OPGx-001 Administered in Patients with LCA5-Associated Inherited Retinal Degeneration (LCA5-IRD). (Protocol V5.2 dated September 4, 2025; Part A Assent ICF dated October 1, 2025; Part A ICF dated November 13, 2025; Part B Assent ICF 13-17 dated October 1, 2025; Part B ICF dated November 3 2025; Part B Assent ICF 13 and younger dated October 1, 2025.)

IBC #25-382, IRB #852708, IND #28950, PROTOCOL #OPGx-LCA5-1001

- Dr. Daniel Kessler introduced the submission.
- Dr. Steven Albelda provided a summary and analysis.
“Project Overview: LCA5 Associated Inherited Retinal Degeneration is a severe, early-onset retinal degeneration with devastating effect on visual function. LCA5 encodes the native human lebercilin protein, which is normally localized to the connecting cilium of photoreceptor cells. This is the stalk between the cell body and the antennae-like outer segments. Disease-causing mutations in LCA5 prevent normal expression of this protein and prevent normal photoreceptor structure and functions leading to blindness. The investigators have shown that subretinal delivery of this AAV (AAV8.hLCA5, now known as OPGx-001) rescued the structure and function of the retina in this model if it was administered at the appropriate dose and at the appropriate time in the disease process (i.e. prior to complete degeneration of the diseased photoreceptors).

A phase 1 trial was approved and began in 2022. Three patients at the first dose have been treated with some evidence of efficacy. Cohorts 2 and 3 (with higher doses), plus pediatric patients are proposed to be treated. This is a renewal of the approved protocol with a number of minor administrative changes and some slight changes in the vision testing protocols. None of these changes has implications for biosafety.

Agent Description: OPGx-001 is a sterile suspension of adeno associated virus 8 (AAV8) serotype vector containing single stranded DNA encoding the unmodified human native LCA5 transgene (pAAV.Hnat.LCA5) driven by a cytomegalovirus (CMV) immediate early enhancer with a chicken beta-actin (C β A) promoter. OPGx-001 is non-integrating and replication incompetent with a genome size of ~4.4 kB.

Is a novel vector system, approach or technology used for this clinical trial? NO

Gene transfer agent delivery method: Subretinal injection done under general anesthesia.

Intended target: Photoreceptor and retinal pigment epithelial cells.

Other material to be used in preparation of the agent: N/A

Potential for shedding: Minimal.

Are “Standard Precautions,” Biosafety Level 2 (BSL-2) equivalent, practices appropriate for ensuring clinical trials personnel safety? **YES**

This Registration Meets IBC Criteria for Approval: **YES.** I recommend approval, as submitted.”

- The new HGT registration was discussed by the committee members.
- All members were in favor of approval.
- The new HGT registration is approved as submitted.

2. Bagley#25-256 C-1

Dr. Stephen Bagley– HGT Protocol Registration Amendment V2**AMENDMENT**
PROTOCOL TITLE: Phase 1b, Open-Label Study of CART-EGFR-IL13Ra2 Cells Administered with Lymphodepleting Chemotherapy or Prior to Surgical Resection in Patients with EGFR-Amplified Recurrent Glioblastoma. (Protocol V2 dated November 10, 2025; Main ICF V2 dated October 23, 2025; Apheresis ICF V2 dated October 23, 2025; Main ICF V3 dated November 11, 2025; Retreatment ICF V2 dated October 23, 2025.)

IBC #25-256, IRB #859355, IND #28055, Sponsor #10325

- Dr. Daniel Kessler introduced the submission.
- Dr. Jessica Buchanan provided a summary and analysis.

“Project Overview: This is an open-label, phase 1b study to evaluate different approaches for CART-EGFR-IL13Ra2 dosing and further characterize the safety, feasibility, preliminary efficacy, and pharmacokinetics of CART-EGFR-IL13Ra2 cells in patients with EGFR-amplified glioblastoma that has recurred following prior radiotherapy. Each dosing approach will be evaluated as a separate treatment arm (Arms A, B, and C). CART-EGFR-IL13Ra2 cells will be administered:

- Arm A: single fixed-dose administration following lymphodepletion.
- Arm B: repeat dose administration following lymphodepletion.
- Arm C: single fixed administration dose prior to surgical resection of the tumor.

Patients will be assigned to each treatment arm sequentially according to their planned treatment date, starting with Arm A. Subjects who demonstrate clinical benefit after initial treatment with CART-EGFR-IL13Ra2 cells may also be eligible to receive treatment with CART-EGFR-IL13Ra2 cells at the physician-investigator’s discretion.

Agent Description: CART-EGFR-IL12Ralpha2 cells are autologous T cells co-expressing two CARs targeting the cryptic EGFR epitope 806 and IL13Ra2. Autologous, patient-derived T cells genetically modified by lentivirus transduction to express a bicistronic CAR transgene from the same transcript, using P2A, the 2A self-cleaving mechanism of the Porcine teschovirus. Each independent CAR transgene consists of an scFv (the human-murine chimeric EGFR scFv specifically binds the conformationally-dependent EGFR epitope 806 and the humanized IL13Ralpha2 scFv specifically binds IL13Ralpha2), a hinge derived from CD8alpha, and a tandem signaling domain comprised of TCRzeta signaling module linked to the 4-1BB costimulatory domain.

Is a novel vector system, approach or technology used for this clinical trial? **NO**

Gene transfer agent delivery method: Intracerebroventricular (ICV) injection.

Intended target: Tumors. Glioblastomas.

Other material to be used in preparation of the agent: N/A

Potential for shedding: N/A

Amendment: This amendment makes the following changes:

- Adds cumulative CART-EGFR-IL13Ra2 data from other studies to the interim review of Arm A data –to ensure that all cumulative data are factored into the decision to open Arm B. Ensures that experience using repeat administration of CART-EGFR-IL13Ra2 in Study #16321/IRB#850297 is appropriately considered prior to opening Arm B..
- Allows for expansion of Arm A up to a total of 8 evaluable subjects if the decision is made to not progress to Arm B.
- Updates the guidance on delaying treatment if patients are positive for respiratory virus other than influenza to better accommodate clinical discretion, in consultation with Sponsor Medical Director, in decision making, given the risks/benefits of delaying study treatment.

No other changes in dosing or safety measures have been made.

Are “Standard Precautions,” Biosafety Level 2 (BSL-2) equivalent, practices appropriate for ensuring clinical trials personnel safety? **YES**

This Registration Meets IBC Criteria for Approval: **YES.** I recommend approval, as submitted.”

- The amendment was discussed by the committee members.
- All members were in favor of approval.
- The HGT registration amendment is approved as submitted.

3. Deik#24-263..... C-1

Dr. Andres F Deik– HGT Protocol Registration Amendment V5 **AMENDMENT**
PROTOCOL TITLE: A Phase 2, Randomized, Double-blind, Sham Surgerycontrolled Study of the Efficacy and Safety of Intraputamenal AAV2-GDNF in the Treatment of Adults with Moderate Stage Parkinson’s Disease. (Protocol V4 dated October 17, 2025; Protocol V5 dated October 24, 205; Main ICF dated March 10, 2025.)
IBC #24-263, IRB #855437, IND #14996, Protocol #ASK-PD5-CS201

- Dr. Daniel Kessler introduced the submission and provided a summary and analysis.

“**Project Overview:** AB–1005 is an investigational gene therapy product being evaluated as a treatment for idiopathic PD and multiple system atrophy-parkinsonian subtype (MSA-P). The gene transfer vector, AAV2-GDNF, is based on a non-replicating form of AAV serotype 2 with an inserted gene encoding normal human GDNF. The AAV2 vector is chosen for its tropism for neurons, as opposed to other cell types within the brain parenchyma.

Following direct administration into the putamen, AAV2-GDNF is taken up by striatal neurons. The transferred DNA encoding GDNF is retained within the host neurons as an episomal DNA within the cell nucleus. Constitutive expression of GDNF within the striatum after AAV2-GDNF administration may provide neurotrophic support to these neurons with durable expression expected to last the remainder of life. GDNF is then secreted to the neighboring substantia nigra pars compacta where the somata of the degenerating DA neurons reside, thereby allowing for neurotrophic support of the full extent of the nigrostriatal pathway.

Approximately 127 participants with moderate Parkinson’s Disease will be randomized in a 2:1 ratio to achieve approximately 114 evaluable participants: 76 in the AAV2-GDNF arm and 38 in the control surgery arm. Randomization will occur on the day of surgery; knowledge of treatment allocation will be restricted to the unblinded teams. Unblinding will occur after the last subject completes the 18-month visit and the database is locked.

For each participant, the study consists of the following periods:

- Screening period – up to 6 weeks
- Baseline period – up to 8 weeks
- Perioperative – approximately 4 weeks
 - Pre-op evaluation
 - Surgical procedure (randomization takes place on same day)
 - Post-op evaluation
- Follow-up (double-blind)
 - Visits will be conducted every 3-6 months and relevant assessments completed
 - Follow-up will end and subsequent unblinding will occur when the last evaluable participant completes the 18-month visit (primary endpoint)

Estimated Overall Study Duration – anticipated duration of 22 to 48 months

Agent Description: AB–1005 (AAV2-GDNF), is a recombinant adeno-associated viral vector serotype 2 (AAV2), encoding the human glial cell line-derived neurotrophic factor (GDNF) protein under the control of the cytomegalovirus (CMV) immediate early promoter. When expressed, GDNF functions to support the survival and promote the differentiation of dopaminergic (DAergic) neurons.

Is a novel vector system, approach or technology used for this clinical trial? NO

Gene transfer agent delivery method: AB–1005 is administered into each putamen using an infusion system consisting of a single use reflux-resistant cannula, a syringe containing AB–1005 dosing solution, and an MR conditional infusion pump. The cannula is made of MR-compatible materials that allow intraoperative MRI monitoring during the dosing procedure.

Intended target: Dopaminergic neurons of the putamen and substantia nigra.

Other material to be used in preparation of the agent: AB–1005 is provided in a sterile formulation of sodium chloride, sodium phosphate, and Poloxamer 188. The excipient for dilution contains the same formulation buffer and will be made by the same manufacturer.

Potential for shedding: Shedding data for AB–1005 have not been collected to date. Biodistribution and shedding of AAV2-GDNF will be evaluated by polymerase chain reaction (PCR) analysis of blood, urine and saliva samples to quantify the presence of the AAV2-GDNF DNA. In consideration of the intracranial route of administration, urine and saliva were selected to assess shedding of AAV2-GDNF. Secondary safety objective.

Amendment: Amendment 5 includes an increase in sample size in increase power of primary endpoint to 95%, revision of secondary and exploratory endpoints to decrease participant burden and align with planned statistical analysis. FDG PET Imaging, previously an exploratory endpoint, removed to help reduce participant burden and radiation exposure risk.

Are “Standard Precautions,” Biosafety Level 2 (BSL-2) equivalent, practices appropriate for ensuring clinical trials personnel safety? **YES**

This Registration Meets IBC Criteria for Approval: YES. I recommend approval, as submitted.”

- The amendment was discussed by the committee members.
- All members were in favor of approval.
- The HGT registration amendment is approved as submitted.

4. McIntosh#25-373C-1

Dr. Paul McIntosh – NEW HGT Protocol Registration **FULL REVIEW**

PROTOCOL TITLE: A single-arm, open-label, dose-escalation study to evaluate the safety, tolerability and efficacy of a single intravenous infusion of AB-1009 in adult participants with late onset Pompe disease (LOPD). (Protocol V3 dated September 24, 2025; Main ICF V1 dated November 17, 2025.)

IBC #25-373, IRB #859843, IND #31472, Protocol #ASK-POM9-CS10

- Dr. Daniel Kessler introduced the submission.
- Dr. Joseph Fraietta provided a summary and analysis.

“**Project Overview:** AB-1009 is a non-replicating recombinant AAV vector for liver-directed expression and secretion of BM40-GAA (secretable, truncated human GAA) under a THBG promoter to provide continuous circulating GAA for systemic cross-correction in LOPD. Adults receive a one-time IV infusion (two dose levels) with prednisone immune prophylaxis and diphenhydramine premedication. Shedding vDNA (blood/saliva/urine) is monitored through Week 24 (or until 3 consecutive negatives), and participants follow protocol-required donation deferral and contraception precautions.

Agent Description: 1. Product / Vector: AB-1009 (AAV-THBG.BM40-GAA), infectious, non-replicating recombinant AAV; ssDNA vector genome flanked by AAV2 ITRs; AAV capsid serotype not specified.

2. Transgene: BM40-GAA (human BM40 signal peptide fused to a truncated human GAA) to promote secretion.

3. Control elements: THBG (liver-specific) promoter; 3' UTR; hGH polyA.

4. Formulation/storage: 20 mM Tris, 0.2 M NaCl, 1 mM CaCl₂, 0.005% poloxamer 188, pH 8.0; stored frozen ≤ -60°C; thaw on wet ice and equilibrate to room temperature.

5. Other elements/handling: AAV2 ITRs only; no wild-type AAV genes; handle using standard universal precautions.

Is a novel vector system, approach or technology used for this clinical trial? NO

Gene transfer agent delivery method: Single IV infusion into a peripheral vein on Day 1. Diphenhydramine 25 mg is given 30 minutes prior and prednisone immune prophylaxis begins Day -1; participants remain inpatient overnight (24 hours) for monitoring.

Intended target: In vivo hepatocyte transduction (THBG promoter) with secretion of BM40-GAA for systemic cross-correction. Human transduction efficiency is not quantified; nonclinical data show liver-predominant biodistribution and dose-related serum GAA activity.

Other material to be used in preparation of the agent: No helper virus or packaging components are used at the clinical site. AB-1009 is supplied as a sterile, vial product and prepared/handled by the pharmacy per the Pharmacy Manual using standard IV supplies.

Routine collection/processing materials include standard supplies for blood, urine and saliva shedding samples and biopsy tissue; handle all as potentially biohazardous per Standard Precautions/BSL-2-equivalent practices.

Summary of preclinical studies: Pompe (GAA KO) mouse studies showed dose-related serum GAA increases and tissue glycogen reductions (MED 5E12 vg/kg). GLP NHP toxicology/biodistribution supported a NOAEL of 5E13 vg/kg with liver-predominant biodistribution and detectable shedding in multiple matrices (including urine/feces and oral/nasal secretions).

Potential for shedding: Potential for shedding. The protocol includes serial vector DNA shedding testing in whole blood, saliva and urine through Week 24 (or until three consecutive negatives). Participants are counseled on 6-month blood/tissue donation deferral and required barrier contraception (theoretical shedding risk). Standard precautions/BSL-2-equivalent practices are appropriate for preparation/infusion and for handling specimens and excreta; ensure clear inpatient and take-home hygiene/waste instructions.

Are “Standard Precautions,” Biosafety Level 2 (BSL-2) equivalent, practices appropriate for ensuring clinical trials personnel safety? **YES**

This Registration Meets IBC Criteria for Approval: YES. I recommend approval, as submitted.”

- The new HGT registration was discussed by the committee members.
- All members were in favor of approval.

- The new HGT registration is approved as submitted.

HGT Administrative Actions: #8

Research Administrative Actions: #54

SECTION III-B. NIH/OBA and IBC Approval Before Initiation

5. Qin25-375B-1, D-4

- The registration was presented by Dr. Tucker Piergallini. This registration is for the generation and/or use of transgenic mice. The lab is interested in studying tissue resident stem cell populations and their offspring in the musculoskeletal system and needs a way to eliminate each cell population of interest from the tissue, without affecting surrounding structures and neighboring cell types. The method selectively activates diphtheria toxin an expression in targeted cell populations, causing their controlled elimination. This is achieved by breeding mice with a conditional DTa gene and Cre-recombinase lines, then inducing expression with Tamoxifen for precise control before analyzing tissue effects. The mice used have been widely employed for decades without reported biosafety concerns. DTa expression is restricted to small cell populations, and any ablated cells are rapidly cleared, eliminating risk of toxin release or systemic effects. Containment has been set to BSL-1 and ABSL-1.
- The registration was discussed by committee members.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

SECTION III-D. Experiments that Require IBC Approval Before Initiation:

6. Atherton22-287D-1,4

- The registration was presented by Ms. Marie-Luise Faber. This registration is for the generation and/or use of retroviral vectors with an amphotropic envelope and was previously tabled by the IBC. This registration is for the use of canine CAR T cells in client owned animals. The lab has updated informed consent form, with guidance similar to animals being treated with chemotherapeutic drugs, has been attached to the registration. Additionally, Dr. Atherton has compiled data from Dr. Mason on RCR and feedback from Penn veterinarians and colleagues performing this type of research. The combined additional information clearly states that the occurrence of RCR after treatment with CAR T cells is extremely low. Containment has been set to BSL-2 and ABSL-1.
- The registration was discussed by committee members.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

7. Edwards25-371D-1,3

- This registration was presented by Ms. Stephanie Adams-Tzivelekidis. This registration is for the generation and/or use of 2nd generation lentiviral vectors. The lab's focus includes noncanonical WNT signaling in proteostasis, regulators of cardiomyocyte contractile/relaxation function, remodeling of cardiomyocytes and other cell types in the heart, and metabolic regulation to unravel the molecular underpinnings of right ventricular heart failure disease of pediatric patients. Additionally, the lab will be using lentivirus that expresses dCas9 KRAB; not active Cas9. Genome editing will not be performed. The listed sgRNA vector will be used to knock-down gene expression via the nuclease-inactive dCas9 fused to the Krüppel-associated box (KRAB) repressor (dCas9-KRAB) to target gene expression via sgRNA. Containment has been set to BSL-2.
- The registration was discussed by committee members. Dr. Daniel Kessler requested the project description include the knockdown cells.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved pending update to project description.

8. Grice25-142D-1,4

- The registration was presented by Dr. Tucker Piergallini. This registration is for the generation and/or use of plasmids in cells and *in vivo*. The lab examines how commensal and virulent bacteria interact with host skin cells *in vitro* and *in vivo*. Plasmids are used to introduce fluorescent (dsRed, dtTomato) and luciferase reporters into *Staphylococcus aureus* for tracking bacterial behavior and host responses. The modified bacteria will be used in human keratinocyte cell lines and mice. Plasmids are sourced from Alex Horswill, University of Colorado and Tom Sutter, University of Memphis. Containment has been set to BSL-2 and ABSL-2.
- The registration was discussed by committee members.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

9. Hogan.....25-265D-1 O-1

10. Hogan.....25-318D-1,4,7

- The registrations were presented by Ms. Marie-Luise Faber. The registrations are for the generation and/or use of 2nd generation lentiviral vector with CRISPR/Cas9 and influenza virus. The lab will transfect murine cells with a 2nd generation lentiviral vector, which has been used previously in similar studies, and they are looking to replicate data and so do not want to change the vector. The work will be *in vitro* only and will deliver a MHC-E receptor protein, where the 3 domain is replaced with that of the classical MHC-I molecule to enable staining with a monoclonal antibody. The transformed cell lines will then be infected with Influenza virus. The lab will generate recombinant influenza virus to study antigen presentation to T cells *in vitro* and in mice to look at immune response. An 8-plasmid system will be used to generate the whole virus in a co-culture of HEK293 and MDCK cells. The lab will infect mouse fibroblasts and primary mouse dendritic cells to conduct biological assays. C57Bl/6 mice will be infected by the intranasal, intramuscular or intraperitoneal route. This will cause an immune response but no disease. Containment has been set to BSL-2 and ABSL-2.

- The registrations were discussed by committee members. Dr. Daniel Kessler requested more descriptive titles for both registrations. Dr. Sara Cherry noted concern for possible gain of function in 25-318 and that the genes of interest were not listed. Dr. Sarah Capasson stated that all gene lists are available through PIERS. Dr. Daniel Kessler confirmed this registration is for novel antigens, loss of function, or partial loss of function. Dr. Sara Cherry requested this be stated in the project description.
- Training was complete.
- All members were in favor of approval.
- The IBC registrations were approved pending updates to titles and project description.

11. Huh25-344D-1,3

- This registration was presented by Ms. Stephanie Adams-Tzivelekidis. This registration is for the generation and/or use of 3rd generation lentiviral vectors. Modified cells were created to support mechanistic and translational studies across multiple organ systems in complex in vitro platforms such as organoids, organ-on-chip, engineered tissues. For example, stable labeling of human endothelial cells with EGFP for live imaging of vascular network formation in co-culture and microfluidic platforms or Reporter assays in human intestinal smooth muscle cells using a smooth muscle myosin heavy chain 11 (MYH11) promoter-enhancer driven EGFP reporter construct to study contractile phenotype and disease. Containment has been set to BSL-2.
- The registration was discussed by committee members. Clarification on the packaging question was requested.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved pending clarification.

12. June25-351D-3,4 O-1

- The registrations were presented by Ms. Marie-Luise Faber. This registration is for the generation and/or use of HSV-1-Based Oncolytic Viruses with gene editing. The lab is looking to develop a more effective cell therapy for solid tumors. The lab will use Herpes Simplex Virus and will utilize engineered Wild-type HSV-1 Strain 17 and the lab strain KOS, which are modified with a combination of genes needed for replication in healthy cells, and support mediating tumor-specificity. Genes of interest will be either deleted or inserted into the HSV genome as described in the registration. The virus will be propagated in Vero cells to generate high concentration virus stock for animal studies, as HSV won't kill the Vero cells. The modified virus will be used to infect and test on human and murine tumor cells that are mentioned in the Target Recipient section. Once in vitro tested yields the preferred response, the modified KOS strain will be injected into mice for desired immune responses and killing of tumor cells. Containment has been set to BSL-2 and ABSL-2.
- The registration was discussed by committee members. Dr. Sara Cherry asked for clarification on use of WT strain of HSV. Ms. Marie-Luise Faber stated WT is only used in tissue culture and not in animal models. Dr. Sara Cherry noted concern for pathogenicity. Dr. Daniel Kessler requested an update to the project description to further define attenuation of the strains.
- Training was complete.
- All members were in favor of approval.

- The IBC registration was approved pending update to the project description.

13. Kreeger25-358D-4

- The registration was presented by Ms. Amanda Wong. This registration is for the generation and/or use of adeno associated viral vectors. The lab aims to identify the neuronal circuits that support hearing by targeting areas of the auditory pathway responsible for encoding sound features critical for speech perception. The lab will focally inject viruses containing transgenes of interest (e.g. fluorescent proteins like GFP, or light-activated ion channels like ChR2) into regions of interest. The modified AAVs are designed to target neuronal populations in the rodent brains. AAVs are purchased through Addgene and are delivered into the brain of mice during sterile stereotaxic surgery using a specialized pump. Containment has been set to BSL-1 and ABSL-1.
- The registration was discussed by committee members.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

14. Morris-Blanco..25-377D-4

- The registration was presented by Ms. Stephanie Adams-Tzivelekidis. This registration is for the generation and/or use of mRNA- LNP. The lab will assess the therapeutic efficacy of lipid nanoparticles (LNPs) encapsulating Cre recombinase mRNA (or noncoding RNA) in a mouse model of ischemic stroke in Ai6 mice. Cre recombinase cleaves DNA at LoxP sites resulting in the expression of ZsGreen fluorescence in Ai6 mice. The mRNA-LNPs will be injected into the brain or intravenously after stroke. The lab will assess the biodistribution of the mRNA-LNPs and therapeutic efficacy by examining 1) brain damage and inflammation via immunofluorescence and histological assessments, and 2) neurobehavioral recovery after stroke. Containment has been set to BSL-1 and ABSL-1.
- The registration was discussed by committee members.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

15. Song25-325D-4

- The registration was presented by Ms. Stephanie Adams-Tzivelekidis. This registration is for the generation and/or use of mRNA- LNP. The lab aims to develop a novel gene therapy strategy to provide a more durable solution for Paroxysmal nocturnal hemoglobinuria (PNH), a blood disorder, where erythroid cells are being destroyed due to the absence of key complement regulatory proteins, such as CD55 and CD59. The lab's approach utilizes lipid nanoparticle (LNP) technology to deliver the mRNA, which encodes for a functional complement regulatory protein, such as CD55 directly to erythroid cells. By transiently expressing the therapeutic protein, this method allows for the targeted correction of the genetic defect in the erythroid lineage and treatment. Containment has been set to BSL-2 and ABSL-1.
- The registration was discussed by committee members.
- Training was complete.

- All members were in favor of approval.
- The IBC registration was approved.

16. Tabrizi.....25-374D-1,3,4 O-1

- The registration was presented by Ms. Stephanie Adams-Tzivelekidis. This registration is for the generation and/or use of 2nd and 3rd generation lentiviral vectors. The lab previously developed antibody-based agents that extend cfDNA circulation time to improve diagnostic sensitivity and now aim to study their effects in cell and animal models. The lab seeks to understand the impact of these agents on innate sensing pathways for dsDNA (e.g. TLR9, cGAS/STING) and the impact of extracellular nucleases (e.g. DNase1L3, DNase 1) on their function. Lentiviral vectors will be used for overexpression of those genes that may affect ctDNA shedding or for the generation of Cas9 expressing cell lines for knockdown experiments of nucleases. Modified cells will be administered to animals via subcutaneous injection. Containment has been set to BSL-2 and ABSL-2.
- The registration was discussed by committee members.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

17. Wilson.....25-396D-1,3 O-1

- The registration was presented by Mr. Edwin Siu. This registration is for the generation and/or use of 3rd generation lentiviral vectors with CRISPR/ Cas 9. The lab works on kidney disease and plans to create an in-vitro model of this by knocking out DCLK1 in cultured human kidney cells using CRISPR-Cas9 in a VSV-pseudotyped 3rd generation lentiviral vector. DCLK1 is an oncogene and is upregulated in kidney cells in chronic kidney disease and is hypothesized to promote inflammation and fibrosis. The generation of these knockouts will allow the group to study the mechanisms responsible for DCLK1-driven kidney injury. Containment has been set to BSL-2.
- The registration was discussed by committee members.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

18. Zaret.....25-362D-4, O-1

- The registration was presented by Ms. Stephanie Adams-Tzivelekidis. This registration is for the generation and/or use of adeno associated viral vectors with CRISPR/Cas 9. The lab uses CRISPR and AAV to mutate, knock out or overexpress genes of interest by direct administration IP, IV, or retro-orbital injections. The genes play an important role in hepatoblast/hepatoblastoma identity maintenance, but also development in the embryo. Containment is set to BSL-1 and ABSL-1.
- The registration was discussed by committee members.
- Training was complete.

- All members were in favor of approval.
- The IBC registration was approved.

SECTION III–O. Experiments that Require IBC Approval Before Initiation:

19. Secreto25-350E-3 O-1

- The registration was presented by Dr. Sarah Capasso. This registration is for the creation of transgenic mice by the Transgenic and Chimeric Mouse Facility (TCMF) and the CRISPR/Cas9 Mouse Targeting Core for the use by the Stem Cell and Xenograft Core (SCXC) staff to provide genetically modified immunodeficient mice as core user need dictates. Transgenic mice may vary so specific genes of interest are not listed. The harvested uterine horns from super ovulated euthanized mice will be used by the TCMF to perform IVF and gene editing, specifically CRISPR/Cas9. Once the transgenes are introduced into fertilized ova, TCMF staff will coordinate surgical implant of embryos into pseudopregnant, SPF recipient females. SCXC in-vivo staff will care for pregnant mice and pups. Containment has been set to BSL-1 and ABSL-1.
- The registration was discussed by committee members.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

20. Wilson.....25-378E-3 O-1

- The registration was presented by Mr. Edwin Siu. This registration is for the creation of transgenic mice by the Transgenic and Chimeric Mouse Facility using AAV vector containing sgRNA targeting DCLK1 and CRISPR-Cas9. The lab investigates how DCLK1 affects kidney disease and plans to generate mice in which DCLK1 is selectively deleted (“knocked out”) only in certain kidney cell types. This doxycycline-inducible selective knockout mouse strain will allow them to study exactly how DCLK1 in specific cells contributes to kidney damage. All the work for generating the mouse strain including vector production will be handled by the Penn IDOM Transgenic and Chimeric Mouse Core. Containment has been set to BSL-1 and ABSL-1.
- The registration was discussed by committee members.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

SECTION III-E. Experiments that Require IBC Notice Simultaneous With Initiation

21. Hogan.....25-266E-1

- The registrations were presented by Ms. Marie-Luise Faber. This registration is for the generation and/or use of BL32 E. coli cells for the chemical transformation of plasmids encoding proteins for functional, structural, and mechanistic studies. The genes being introduced will target the MHC-E receptors to analyze binding affinity, structure, and mechanistic functions with modifications only effecting the ability of the protein to be stably folded with and without a peptide loaded

- The registration was discussed by committee members
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

3. New Business:

- (a) No New Business Scheduled.

4. Old Business:

- (a) No Old Business Scheduled.

5. End Meeting:

- The Institutional Biosafety Committee was adjourned by Dr. Daniel Kessler at **10:57 AM**.

Our next meeting scheduled for Monday, January 26th, 2026, will be held on site at the EHRS Office with a Teleconference option, at 10:00 am. A light Brunch will be provided.