

Institutional Biosafety Committee:

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

Absent: Dr. Steven Albelda, Dr. Paul Bates, Dr. Joseph Fraietta, Dr. Maureen O’Leary

Invited Guests: Ms. Stephanie Adams, Ms. Marie-Luise Faber, Dr. Tucker Piergallini, Ms. Amanda Wong, Ms. Kimberly Craig, Mr. Tony Secreto

The Institutional Biosafety Committee Meeting was called to order by Dr. Daniel Kessler at **10:01 AM**.

1. IBC Minutes: **09-22-2025**

- 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. Frank#23-063 C-1

Dr. Ian Frank– HGT Protocol Registration Amendment V6 **AMENDMENT**

PROTOCOL TITLE: A Phase 1, Randomized, Double-Blind, Placebo-Controlled Clinical Study to Evaluate the Safety, Reactogenicity and Immunogenicity of the HCMV-HIV Vaccine Candidate VIR1388 in Adult Participants with Overall Good Health and Without HIV. (Protocol V6 dated June 17, 2025; Pregnancy IF dated September 3, 2025; Follow Up ICF dated September 3, 2025; Long Term Follow Up dated September 3, 2025.)

IBC #23-063, IRB #853495, IND #029250, PROTOCOL #HVTN 142/VIR-1388-V101

- Dr. Daniel Kessler introduced the submission.
- Dr. Steven Albelda provided a summary and analysis. This submission was read into record by Amada Wong.

“Project Overview: No candidate human immunodeficiency virus (HIV) vaccine has ever shown more than marginal protection against HIV infection in Phase 3 efficacy studies. VIR-1388 is CMV-based HIV vaccine candidate that offers a novel mechanism of protection against HIV in preclinical models. This study will evaluate the safety and reactogenicity of VIR-1388 compared to placebo when administered subcutaneously in health human Cytomegalovirus (HCMV)-seropositive adult participants. The protocol has been previously approved. This amendment contains a number of administrative changes, many of which include changes in wording necessitated by the recent presidential executive order. The other changes was to reflect the change in study sponsorship from Vir Biotech to the Division of AIDS at NIAID and to align protocol language with standard DAIDS processes.

Agent Description: VIR-1388 is an HCMV-HIV vaccine vector engineered deliver immunogens relevant to the therapeutic and/or prophylactic indication. All clinical study materials are manufactured in accordance with current Good Manufacturing Practice (cGMP) regulations.

The following further changes were made to the HCMV vector backbone in VIR-1388 with the potential to enhance immunogenicity and support future development:

1. Deletion of UL18.
2. Choice of UL78 instead of UL82 for transgene insertion.
3. The Mfuse1 transgene in VIR-1388 is an antigen designed to elicit broad immune coverage against circulating HIV strains, as compared to the antigenic insert in VIR-1111, which represents only 1 HIV clade. The Mfuse1 transgene was designed using an epigraph strategy to capture the most common overlapping 9 amino acid sequences in the HIV proteins Gag, Pol and Nef, based on the full-length protein for each of several hundred

thousand unique HIV isolates in the HIV sequence database. The breadth of potential T cell epitopes in Mfuse1 is predicted to elicit CD4 and CD8 T cells that recognize proteins from many HIV strains.

Is a novel vector system, approach or technology used for this clinical trial? YES

Gene transfer agent delivery method: Subcutaneous injection.

Intended target: Uptake by dendritic cells and other white blood cells with presentation of antigen in lymph nodes.

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

Preclinical studies: There has been some clinical experience with this vector. It has been given to more than 25 patients without any serious adverse events.

Potential for shedding: Yes, this is being assessed in the protocol. No concerns.

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.

2. Frank#24-265 C-1

Dr. Ian Frank – HGT Protocol Registration Amendment V3 **AMENDMENT**

PROTOCOL TITLE: HVTN 312: A Phase 1 clinical trial to evaluate the safety and immunogenicity of CH505M5 N197D mRNA-gp160 followed by CH505 TF mRNA-gp160 in adults in overall good health without HIV. (Protocol V3 dated August 28, 2025; Main ICF dated September 23, 2024.)

IBC #24-265, IRB #856746, IND #030827, PROTOCOL #HVTN312

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

“Project Overview: The HVTN 312 is a multicenter, open-label, non-randomized, dose escalation, first in human Phase 1 study designed to determine the ability of CH505M5 N197D mRNA-gp160 to expand pools of precursors of VH1-46 CH235-like B cells with mutations of early intermediates of CH235 lineage bnAbs. A second goal is to determine if the sequential boosting with CH505 TF mRNA-gp160 and CH505 w24 mRNA-gp160 will select for functional bnAb mutations in intermediate CH235-like bnAb lineage BCRs that occur after the priming immunogen. All 3 study products in this study are mRNA encapsulated in LNPs. The CH235 class of bnAbs has been identified as an attractive pathway for focused vaccine development to elicit CD4-mimicking bnAbs in people living without HIV, exhibiting strong neutralization breadth and potency. This bnAb class exclusively uses the VH1-46 heavy chain gene and does not depend upon insertions or deletions, which are rare events, for maturation.

Agent Description: CH505M5 N197D mRNA-gp160 (Prime): The priming immunogen, CH505M5 N197D mRNA-gp160, is an LNP-encapsulated mRNA encoding a high affinity CH505M5 gp160 Env Trimer which contains the N279K, G458Y and N197D mutations, as well as a stabilizing I535M mutation. The in vivo expressed protein will be anchored in the membrane of cells that take up the mRNA-LNP.

CH505 TF mRNA-gp160 (Boost 1): The first boosting immunogen, CH505 TF mRNA-gp160, is an LNP-encapsulated mRNA encoding a high affinity CH505 gp160 Env Trimer. CH505 TF mRNA-gp160 encodes the wildtype TF sequence and lacks the N279K, G458Y, N197D and I535M mutations contained in CH505M5 N197D mRNA-gp160. The encoded amino acid sequence thus differs from the prime by 4 amino acids. Like the priming immunogen, the expressed protein will be anchored in the membrane of cells that take up the mRNA-LNP.

CH505 w24 mRNA-gp160 (Boost 2): The second boosting immunogen, CH505 w24 mRNA-gp160, is an LNP-encapsulated mRNA encoding a high affinity CH505 gp160 Env Trimer. CH505 w24 mRNA-gp160 encodes the CH505 Env with additional mutations designed to further mature the CH235 bnAb lineage. Like the other immunogens, the expressed protein will be anchored in the membrane of cells that take up the mRNA-LNP.

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

Gene transfer agent delivery method: Lipid Nano Particle-encapsulated mRNA. The Phase 1 clinical doses will be 25, 50, 100 or 150 mcg for all three vaccines. Study product will be diluted and administered as two separate 0.25 mL injections IM into each deltoid muscle (both left and right) by needle and syringe..

Intended target: LNPs are targeted to the deltoid muscle, which will be the primary site of antigen expression.

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

Preclinical studies: N/A

Potential for shedding: N/A

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. Frey.....#23-185..... C-1

Dr. Noelle Frey– HGT Protocol Registration Amendment V9 **AMENDMENT**

PROTOCOL TITLE: UPCC 26423 Phase 1 Study of Lentivirally Transduced T Cells Engineered to Contain Anti-CD33 Linked to TCR and 4-1BB Signaling Domains in Combination with CD33KO-HSPC in Subjects with Refractory or Relapsed Acute Myeloid Leukemia. (Protocol V9 dated August 7, 2025; Donor ICF dated August 7, 2025; Recipient ICF dated August 7, 2025.)

IBC #23-185, IRB #854325, IND #29490, UPCC #26423

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

“Project Overview:

This is a phase 1 study to determine the safety, manufacturing feasibility, and efficacy of CD33KO-HSPC followed by CART-33 cells in subjects with relapsed/refractory AML. The primary objective of the study is to assess safety and manufacturing feasibility. Up to 16 subjects will be enrolled for a total of 8 evaluable subjects. Evaluable subjects are those who have received alloHSCT with CD33KO-HSPC.

AML accounts for approximately 33% of all leukemias, with 19,940 new cases and 11,180 deaths annually, as of 2020, as reported in the United States [American Cancer Society, Cancer Facts and Figure 2020. Atlanta: American Cancer Society, 2020]. AML is the most common acute leukemia in adults, with an incidence of 3-5 per 100,000 population.¹ The only subjects with refractory (active) disease who experience meaningful long-term leukemia-free survival are those who undergo allogeneic hematopoietic cell transplantation (alloHSCT). Even in this setting, only select subjects enjoy a median Overall survival exceeding 1 year (Figure 5).³

CD33 on AML, but also on HSC. So need a way to kill tumor cells without HSCs.

Agent Description:

- **CD33KO-HSPC (Product 1):** AlloHSCT with CD34-selected HSPC that have been edited ex vivo to knockout CD33 using CRISPR-Cas9. HSPC will be obtained via peripheral blood apheresis from the donor after granulocyte colony stimulating factor (G-CSF) and plerixafor mobilization. Cells will undergo CD34 selection using magnetic beads, followed by electroporation with guide ribonucleic acid (gRNA) targeting exon 2 of CD33, pre-complexed with Cas9 protein.

- **CART-33 (Product 2)** will have been manufactured from the peripheral blood mononuclear cells (PBMC) from the same allogeneic donor from whom CD33KO-HSPC are generated. T-cells will be collected at steady state from the donor, prior to any G-CSF therapy and then lentivirally transduced with a construct comprising an anti-CD33 CAR single chain variant fragment, the CD3 ζ signaling molecule and the 4-1BB costimulatory domain.

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

Gene transfer agent delivery method: CD33KO-HSPC (Product 1): Desired dose for infusion is 2x10⁶/kg, with a minimum acceptable dose of 1x10⁶/kg CD33 deficient CD34+ cells after conditioning chemo/radiotherapy.

CART-33 (Product 2): Allogeneic CART-33 cells will be administered on a fractionated schedule, beginning no earlier than 4 weeks after alloHSCT, provided engraftment has occurred and acute transplant-related toxicities have resolved. CART infusion may be preceded by lymphodepleting chemotherapy.

Intended target: relapsed/refractory AML Adult subjects with AML at high risk of relapse post alloHSCT, defined as having detectable AML at time of enrollment despite appropriate prior therapy.

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

Preclinical studies: N/A

Potential for shedding: N/A

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

Summary of protocol amendment: Changes include: Clarification of eligibility. Updated safety review. Updated thaw process per manufacturer. Administrative changes.

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. Haas#25-179C-1

Dr. Andrew R Haas– HGT Protocol Registration Amendment V3 **AMENDMENT**

PROTOCOL TITLE: Phase I Clinical Trial of Autologous Folate Receptor-Alpha Redirected T Cells in Patients with FRa+ Cancers. (Protocol V3 dated October 1, 2025; Main ICF V3 dated October 1, 2025)

IBC #25-179, Sponsor# 06525, IRB# 858800, IND # 14802

- Dr. Daniel Kessler introduced the submission.
- Dr. Joseph Fraietta provided a summary and analysis. This submission was read into record by Amada Wong.

“Project Overview: T Evaluate safety/tolerability, feasibility, and preliminary anti-tumor activity of IP MOv19-BBz CAR T cells for FRa-positive malignancies with pleural effusions; exploratory work includes pharmacokinetics/persistence, bioactivity, and TME characterization. Subjects may initiate checkpoint inhibitor (CPI) therapy after Day 28, with primary follow-up aligned to CPI cycle timing when applicable.

Agent Description: Source/Vector System (ex vivo): Autologous T cells lentivirally transduced to express the MOv19-BBz CAR; manufactured at UPenn CVPF; cryopreserved in infusion bags.

Construct/Modifications: MOv19 scFv (murine origin) targeting FRa, fused to 4-1BB co-stimulatory and CD3ζ signaling domains (human intracellular sequences). Expression platform per Penn’s lentiviral system (EF-1α is used in preclinical development referenced in protocol).

Transgene/Cargo: CAR sequence encoding MOv19 scFv 4-1BB-CD3ζ to redirect autologous T cells toward FRa-expressing tumor cells.

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

Gene transfer agent delivery method: Single intrapleural (IP) infusion on Day 0, 3 days (±1) after completion of lymphodepleting chemotherapy: fludarabine 30 mg/m²/day ×3 (rounded down to nearest 50 mg if within 10%) and cyclophosphamide 300 mg/m²/day ×3. Recommended infusion: 10–20 mL/min. Outpatient administration is expected; inpatient at investigator discretion. Dose Level 1 (DL1): 5×10⁷ CAR⁺ cells; if >2 TLTs occur at any time, de-escalate to DL-1: 2.5×10⁷. Minimum acceptable dose for infusion: 2.5×10⁷.

Intended target: Ex vivo lentiviral transduction of autologous T cells; in vivo target is FRa on tumor cells in the pleural space. Preclinical data support FRa-specific lysis and activity; clinical-grade transduction efficiency varies by lot (platform typically supports robust CAR expression)

Other material to be used in preparation of the agent: Onsite handling is limited to the cryopreserved CAR T cell product. Cryomedia per protocol includes CryoStor®/PlasmaLyte A; an alternative cryopreservation formula (with 7.5% DMSO and Dextran-40) may be used; hypersensitivity to excipients is an exclusion. Lymphodepleting agents are standard sterile products from pharmacy.

Preclinical studies: Protocol summarizes FRa CAR in vitro cytotoxicity and cytokine data, xenograft anti-tumor activity, and route comparisons; prior MOv19-BBz intraperitoneal experience informed dose selection.

Potential for shedding: No replicating vector is administered at the bedside; persistence relates to genetically modified T cells, monitored by qPCR in blood (and pleural fluid research samples). RCL testing is not routine; blood is banked for RCL testing if indicated. Recommend ensuring closed-system pleural drainage and BSL2-equivalent precautions for pleural effluent during the immediate post-infusion period.

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

Summary of protocol amendment: Key elements retained: Single-dose IP MOv19-BBz after Cy/Flu LD; staggered dosing; Day-28 TLT window; option to de-escalate from 5×10⁷ to 2.5×10⁷ if safety triggers met; CPI allowed after Day 28.

The proposed amendments to the protocol are as follows:

1. Staggering & decision points clarified. First two subjects per dose level must be staggered by ≥28 days; additional stagger after the 3rd subject to complete a formal TLT evaluation and confirm next dosing; at DL-1, if 1/3 TLT occurs, perform TLT review after each additional subject and do not start LD for the next subject until the preceding subject completes Day-28 safety window.
2. TLT criteria refined. Adds explicit exceptions (e.g., Grade 3 hypoxia needing low-flow O₂ <6 L/min not automatically TLT; isolated Grade 3/4 lab abnormalities that improve to ≤Grade 2 or baseline within 7 days; etc.). Clarifies that CRS component events (hypotension/hypoxia) are not independently evaluated against TLT if captured under the CRS diagnosis.
3. Pause/stop rules expanded. Any treatment-related death within Day-28, any death ≤30 days unless clearly due to progression, any Grade 4 IEC-HS, Grade 4 CAR neurotoxicity with cerebral edema, two Grade 4 CRS/ICANS, two TLTs at DL-1, RCL detection (testing if suspected; samples banked), and new possibly related malignancy trigger pause/review.
4. CPI integration after Day 28. Primary follow-up aligns with CPI cycles (e.g., Cycle X/Day 1 documented alongside study day), with imaging typically every 2-4 cycles per routine care; if CPI stops, subject transitions to LTFU schedule.

5. Schedules & LTFU. Appendix schedules clarify monthly visits Months 2-6, quarterly Months 9 and 12, and LTFU through Year 15. Loss of persistence requires two sequential negative qPCR tests before reducing frequency; subjects without progression who enter LTFU continue response evaluations (minimum q6 months) until documented post-CAR progression.
6. Manufacturing/handling detail. Lists an alternative cryopreservation composition (with DMSO/Dextran-40) and re-states labeling/bedside thaw/infuse within 60 min of thaw practices.
7. Dose rounding detail. Fludarabine rounding down to nearest 50 mg vial if within 10% of prescribed dose is specified in dosing tables and LD sections.
8. Infection screening & prophylaxis more explicit. RVP (inclusive of SARS-CoV-2) within 14 days prior to LD/CAR T, with delay rules for positives; outlines post-LD prophylaxis expectations (gram-negative coverage; PJP/HSV/fungal when using Flu).
9. Safety frameworks and references updated. Protocol embeds ASTCT grading for CRS/ICANS, formalizes IEC-HS framework, and adds recent long-term safety literature citations in references.

Biosafety Summary and Recommendation: The amendment does not change the underlying biosafety profile: the investigational product is ex vivo modified, autologous T cells; no replication-competent viral vector is administered. Monitoring for product persistence and late effects is reinforced through the clarified follow-up/LTFU plan (including qPCR-based persistence rules), and RCL detection is an explicit pause/stop trigger with samples banked for testing if suspected. Staff exposure risks remain routine for cellular therapies including cryobag handling, body-fluid contact, and pleural drainage/waste and are appropriately addressed by Standard Precautions/BSL-2-equivalent practices. The amendment strengthens safety oversight (clear staggering/decision points, refined TLT criteria, expanded pause/stop rules, and updated ASTCT CRS/ICANS/IEC-HS frameworks) and clarifies manufacturing/handling (alternative cryopreservation; thaw/infuse within 60 minutes). Pre-LD infection controls are made more explicit (RVP within 14 days, delay rules; post-LD prophylaxis expectations). Overall, these changes tighten controls without introducing new biosafety hazards to personnel, subjects, or the community. Thus, this reviewer recommends approval of the amendment as submitted.

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.

5. Nasta#25-300 C-1

Dr. Sunita D Nasta- NEW HGT Protocol Registration..... **FULL REVIEW**

PROTOCOL TITLE: UPCC 54425: The CAROLYN Trial: Lisocabtagene Maraleucel as First-Line Therapy for Primary Central Nervous System Lymphoma (PCNSL) in Transplant-Ineligible Patients. (Protocol V1 dated Marh 29, 2025; Main ICF dated May 19, 2025.)

IBC #25-300, IRB #859335, IND # 016506, Protovol# CA0821215

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

“**Project Overview:** Primary Central Nervous System Lymphoma (PCNSL) is a rare and aggressive form of non-Hodgkin lymphoma (NHL) which is confined to the brain, spinal cord, and leptomeningeal or vitreoretinal space. It us a distinct class of hematopoietic and lymphoid tumors and accounts for approximately 3% of all neoplasms and 4% to 6% of all extranodal lymphomas. The prognosis of elderly/frail patients with PCNSL who are deemed transplant-ineligible is heavily altered by the absence of consolidation with high-dose chemotherapy/autologous stem-cell transplantation, with outcomes inferior to their transplant-eligible counterparts; hence, this population is in need for novel therapeutic strategies.

Targeting of CD19 with CAR T-cells has demonstrated deep and durable responses in the treatment of various B-cell lymphomas, including PCSNL and secondary CNS lymphoma. Currently, there are no CAR T-cell therapy treatments approved for PCNSL in the front-line or relapsed/refractory setting; however, published experiences evaluating its use in the relapsed/refractory setting have been reported, confirming its safety and feasibility, including liso-cel. Furthermore, these data may support potential to demonstrate improved efficacy in PCNSL versus current standard of care options. More importantly, this may be a preferred clinical option in the defined patient population of PCNSL able to receive induction therapy consisting of high-dose methotrexate (HDMTX) but deemed transplant-ineligible for consolidative HDCT/ASCT.

Approximately 65 participants with PCNSL will be enrolled on to this open-label, multicenter, Phase 2 study to evaluate the safety and efficacy of liso-celin adults as first-line treatment in transplant-ineligible PCNSL.

Agent Description: The liso-cel investigational drug product is composed of autologous CD8+ and CD4+ T cells that express a CD19-specific CAR. The CD19-specific CAR is introduced into autologous CD8+ and CD4+ T cells ex vivo using a replication-incompetent, self-inactivating lentiviral vector. The CD19-specific CAR consists of a scFv binding domain derived from a murine CD19-specific mAb, IgG4 hinge region, CD28 transmembrane domain, 4-1BB costimulatory domain, and CD3 zeta activation domain. The EGFRt protein is co-expressed with the CD19-specific CAR as a cell surface protein.

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

Gene transfer agent delivery method: Intravenous infusion of CAR-T product.

Intended target: Lymphoma cells expressing the CD19 antigen in vivo.

Other material to be used in preparation of the agent: Manufacturing and Formulation: Liso-cel is manufactured using standard CAR-T methods. CD4 and CD8 T-lymphocytes are collected from subject leukapheresis material. Following isolation and activation cell culture is initiated and cells are transduced with LVV to express the CD19 CAR and expanded for 4 days. The cells are then washed and concentrated to make CART19, which is a cryopreserved liquid cell suspension intended for intravenous infusion.

Preclinical studies: N/A

Potential for shedding: N/A

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.

6. Schuster.....#24-032..... C-1

Dr. Stephen J Schuster – HGT Protocol Registration Amendment V3 **AMENDMENT**

PROTOCOL TITLE: UPCC 02424: A Phase 1b Multicenter, Open-label, Study of JNJ-90009530, an Autologous Anti-CD20 CAR-T Therapy in Adult Participants with Relapsed or Refractory B-cell Non- Hodgkin Lymphoma. (Protocol V3 dated November 8, 2024; Main ICF dated November 26, 2024.)

IBC #24-032, IRB #855375, IND #028963, PROTOCOL #JNJ-90009530

- Dr. Daniel Kessler introduced the submission.
- Dr. Maureen O’Leary provided a summary and analysis. This submission was read into record by Amada Wong.

“Project Overview: This is a Phase 1b multicenter, open-label study sponsored by Janssen Research & Development, LLC and designed to assess the safety and tolerability of JNJ-90009530 (formerly known as C-AR066), an autologous chimeric antigen receptor (CAR) T cell therapy targeting CD20 in adult participants with relapsed or refractory B-cell non-Hodgkin lymphoma (r/r B-NHL). This trial has a target enrollment of approximately 52 participants.

Agent Description: The study agent JNJ-90009530 consists of autologous T lymphocytes transduced with a recombinant, replication-defective lentiviral vector designed to express a novel 2nd generation CAR-T construct targeting CD20.

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

Gene transfer agent delivery method: Infusion.

Intended target: relapsed or refractory B-cell non-Hodgkin lymphoma (r/r B-NHL).

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

Preclinical studies: N/A

Potential for shedding: N/A

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

Summary of protocol amendment: In this amendment version 3 there are mostly administrative changes. The most significant change in this amendment improves the safety of the study because Long-term Follow-up has been added and defined as: “All participants who received JNJ-90009530 will continue to be monitored for long-term safety up to 15 years after the last participant has been administered JNJ-90009530.

Participants in the long-term follow-up will be monitored annually for clinical, safety, pharmacokinetics, biomarker assessments and survival status. Annual clinical assessments (hematology, chemistry, vital signs, and physical examination) will be required through Year 5 after CAR-T infusion.

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.

7. Tanyi.....#25-055..... C-1

Dr. Janos Tanyi HGT Protocol Registration Amendment V13 **AMENDMENT**

PROTOCOL TITLE: UPCC 37824 / IMA203-101: Phase 1/2 study evaluating genetically modified autologous T cells expressing a T-cell receptor recognizing a cancer/germline antigen as monotherapy or in combination with nivolumab in patients with recurrent and/or refractory solid tumors (ACTengine IMA203-101). (Protocol V13 dated June 17, 2025; Main ICF V12 dated June 25, 2025.)

IBC #25-055, IRB # 857729, IND IMA203: 018491, IND IMA203CD8: 028316, Protocol #IMA203-101

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

“Project Overview: This clinical study is a multicenter, open-label, 3 + 3, dose-escalation/de-escalation, first in human Phase 1/2 study to evaluate the safety, tolerability, and preliminary anti-tumor activity of treatment with IMA203 (autologous PRAME-specific T cells) and IMA203CD8 (autologous PRAME-specific T cells, additionally co-transduced with a vector that codes for a CD8 $\alpha\beta$ co-receptor) in patients with PRAME-positive recurrent and/or refractory solid tumors.

PRAME is a cancer-testis antigen, expressed in both cancer cells and germ cells. It is particularly overexpressed in several types of cancer, including: melanoma, leukemia, Ewing sarcoma, and germ cell tumors. Eligible patients must be HLA-A*02:01 positive with solid cancers whose tumors express PRAME.

The primary aim of the P1 study is to evaluate safety and tolerability of treatment with IMA203/IMA203CD8 products as monotherapy or in combination with nivolumab (check point inhibitor) using up to 6 ascending dose levels and to determine the maximum tolerated dose (MTD) and/or recommended Phase 2 dose for extension (RP2D). At the time of this protocol amendment, DL5 of IMA203 has already been cleared for safety (0/6 patients with DLT).

After determination of the final MTD/RP2D, two disease-specific extension cohorts may be initiated in the P2 extension part of the study, where patients will be enrolled and treated with the final MTD/RP2D in "tumors of special interest" TOSI cohort I (patients with cutaneous or uveal melanoma) or TOSI cohort II (patients with ovarian/fallopian tube cancer, or uterine corpus endometrial cancer, and uterine carcinosarcoma).

As of 07-Apr-2025, a total of 74 patients have been enrolled in the trial with manageable and acceptable tolerability and safety profile, as well as promising efficacy data. By the cut-off date for that analysis (07-Apr-2025), observed complete objective response rate in melanoma patients treated with IMA203 during dose expansion at RP2D (n=33) was 56% (18/32 evaluable patients). Median duration of response was 12.1 months with 8/18 confirmed responses ongoing (longest 33 months after infusion).

IMA203CD8 is also being investigated, and in P2, this product will focus on tumors with unmet medical need and high and uniform PRAME expression and high and uniform PRAME expression. Results from these cohorts will be primarily used to generate additional safety data and preliminary efficacy data in these selected tumor types that prevalently express PRAME.

Agent Description: Each IMA203 CAR T-cell product is a cell suspension that contains engineered T-cells expressing T cell receptor specific to PRAME-004 target peptide presented by HLA-A*02:01 engineered using a third-generation lentiviral vector system.

IMA203CD8 is an autologous T cell product engineered to express the PRAME-specific T cell receptor used for IMA203 and in addition the CD8 co-receptor to overcome the lack of functionality among the TCR-transduced CD4+ T cells. The CD8 $\alpha\beta$ co-receptor is co-transduced during the production process of IMA203CD8 to re-direct also CD4+ T cells towards the HLA class I-restricted PRAME antigen.

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

Gene transfer agent delivery method: Third generation lentivirus vector.

Intended target: Target cells overexpressing PRAME peptide/cancer antigen in the context of HLA-A*02:01.

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

Preclinical studies: N/A.

Potential for shedding: No concern for vector shedding. Investigator brochures and study protocols for IMA203 and IMA203CD8 version 13 have been updated to include administrative changes that do not impact the safety of the CAR T cell product.

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.

8. Tebas#25-285..... C-1

Dr. Pablo Tebas – NEW HGT Protocol Registration **FULL REVIEW**

PROTOCOL TITLE: A Phase 1, Open-Label, Single Center, Dose Escalation Study of the Safety and Pharmacokinetics of mAb AZD5396 and mAb AZD8076 delivered as dMAbs in Healthy Adults. (Protocol V11 dated April 26, 2024; ICF Cohorts A1-D V12 dated Jan 30, 2024; ICF Cohorts E-G V4 dated January 30, 2024; Sub-Study ICF VA2 dated July 17, 2025.)

IBC #25-285, IRB #850355, IND #28225, PROTOCOL #SARS-CoV-2-dMAb01

- Dr. Daniel Kessler introduced the submission.
- Dr. Andrew Maksymowych provided a summary and analysis. This submission was read into record by Amada Wong.

“Project Overview: This trial proposes the use of DNA-encoded monoclonal antibodies (dMAbs) to provide pre-exposure prophylaxis against SARS-CoV-2. dMAbs are a unique synthetic nucleic acid platform for in vivo delivery of protective mAb providing a broad countermeasure for COVID-19 infection.

Achieving consistent, high in vivo expression levels is the major technical challenge with most gene encoded antibody platforms. To address this challenge, our team has invested significant resources in the areas of 1) sequence optimization; 2) formulation optimization; and 3) delivery optimizations in large animal models such as non-human primates (NHPs) and pigs. As part of SARS-CoV-2 dMAb

preclinical development, we will employ these three strategies to ensure high levels of in vivo expression.

This study directly addresses the need for preventative medical countermeasures against SARS-CoV-2.

dMAbs have the potential to be delivered as pre-exposure prophylaxis to at-risk populations such as the warfighter and other military personnel, health-care workers, and other vulnerable populations such as the elderly, also in combination with vaccination. In addition to prevention, dMAbs may be a treatment option for exposed individuals.

Agent Description: dMAb-AZD5396 & dMAb-AZD8076

DNA-encoded monoclonal antibody dMAb-AZD5396

DNA plasmids pGX93321 and pGX93311 are synthetic constructs derived from the monoclonal antibody 2130, which was isolated from a human subject previously infected with SARS-CoV-2. The highly optimized engineered sequence of pGX93321 encodes the heavy chain and that of pGX93311 encodes the light chain of mAb-AZD5396 respectively. Both the heavy and light chains in pGX93321 and pGX93311 are driven by a human CMV (hCMV) promoter with the bovine growth hormone 3'end poly-adenylation (bGH polyA) signal.

DNA-encoded monoclonal antibody dMAb-AZD8076

DNA plasmids pGX93322 and pGX93315 are synthetic constructs derived from the monoclonal antibody 2196, which was isolated from a human subject previously infected with SARS-CoV-2. The highly optimized engineered sequence of pGX93322 encodes the heavy chain and that of pGX93315 encodes the light chain of mAb-AZD8076, respectively. Both the heavy and light chains in pGX93322 and pGX93315 are driven by a human CMV (hCMV) promoter with the bovine growth hormone 3'end poly-adenylation (bGH polyA) signal.

The backbone used to construct the plasmids pGX93322 and pGX93315 is pGX0001, which was derived from a commercially available pVAX1 plasmid. pGX0001 is under the control of the human CMV promoter and includes the kanamycin resistance gene and plasmid origin of replication (pUC ori).

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

Gene transfer agent delivery method: CELLECTRA™ 2000 – Electroporation

The investigational device used in the study is the CELLECTRA™ 2000 with Side Port Needle.

The CELLECTRA™ 2000 with Side Port is a portable, battery-powered medical device designed to generate a minimally controlled, electric field which temporarily and reversibly increases cellular membrane permeability without damaging the tissue. During the period of increased permeability an indicated injected plasmid DNA formulation can be introduced into the cells.

The device is indicated to enhance the uptake and expression of DNA plasmid-based biologics in order to enhance vaccine efficacy. The DNA plasmid is delivered separately via needle and syringe injection in the area delineated by the electrodes immediately prior to the electroporation treatment. The electroporation is accomplished through a sterile, disposable needle array attached to an applicator delivering pulsed electrical currents.

Intended target: The intended target is **SARS-CoV-2 Virus**

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

Preclinical studies: N/A

Potential for shedding: Material administered is nucleic acid (plasmid DNA) to produce monoclonal antibodies in vivo. Shedding is not a biosafety concern.

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.

9. Tebas#25-293..... C-1

Dr. Pablo Tebas – NEW HGT Protocol Registration **FULL REVIEW**

PROTOCOL TITLE: Phase I, randomized, observer-blinded, placebo-controlled, 2-part, dose escalation and expanded safety evaluation trial to evaluate the safety, tolerability and immunogenicity of an investigational prophylactic vaccine for the prevention of genital lesions caused by HSV-2 and potentially HSV-1. (Protocol V11 dated May 15, 2025; Main ICF dated June 18, 2025.)

IBC #25-293, IRB #852362, IND #28577, PROTOCOL #BNT163-01

- Dr. Daniel Kessler introduced the submission.
- Dr. Andrew Maksymowych provided a summary and analysis. This submission was read into record by Amada Wong.

“Project Overview: Genital infection caused by HSV-2 now affects 500 million people, and HSV-1 genital herpes affects more than 140 million people worldwide. Painful genital lesions, emotional distress because of concerns about transmitting infection to intimate partners or neonates, active genital lesions in pregnancy increasing the risk of congenital anomalies, increased risk for human immunodeficiency virus (HIV) acquisition, and increased risk of sporadic meningitis are several of the serious clinical sequelae of herpes infections. Both condoms and antiviral drugs are estimated to reduce transmission by ~50% when frequently used; but drug resistance is increasingly documented, and currently approved interventions are not failsafe as they are dependent on user compliance and do not prevent viral shedding and transmission. Thus, use of pre- or post-exposure prophylaxis could never replace the benefit derived from a safe and effective prophylactic herpes vaccine.

No vaccine has been licensed for prevention of genital lesions caused by HSV to date, despite extensive efforts by major pharmaceutical companies evaluating various subunit vaccine candidates through to large Phase III trials.

This exploratory trial will have three parts.

Part A will focus on safety evaluations, and in addition, vaccine-induced immune responses (specifically neutralizing antibodies) will be analyzed to assess if there is a dose-response.

Part B of the trial will expand the safety characterization for two BNT163 dose levels (30 µg and 60 µg) selected based on Part A data and will also enable a more comprehensive assessment of the impact of pre-existing immunity to HSV-1 and -2 on the safety and immune responses to BNT163.

Part C will evaluate safety and immunogenicity of 60 µg BNT163 compared to a placebo in a threedose regimen in subjects with a history of HSV-2 recurrent genital herpes. Three doses of BNT163 will be given to assure vaccine-related memory responses and to assess the differences in individuals without recurrent genital herpes compared to individuals with recurrent genital herpes following immune challenge (Dose 1) and booster doses (Doses 2 and 3) with BNT163.

Agent Description: BNT163

BNT163 uses lipid nanoparticles (LNPs) to deliver RNA to cells, where it is used to express proteins for the prophylactic effect.

The RNA drug substance of BNT163 is 1:1:1 mixture of three highly purified single-stranded, 5'-capped nucleoside-modified RNAs. The RNA drug substance is produced by in vitro transcription from DNA templates. There are three RNAs in BNT163, each encode one of three HSV-2 glycoprotein ectodomains – C, D, and E (gC2, gD2, gE2). An encoded secretory signal peptide guides translocation of the nascent protein for further processing.

The drug product is a preservative-free, sterile suspension/dispersion for dilution for IM administration. The drug product contains RNA (the drug substance) formulated in LNP in aqueous cryoprotectant buffer. The composition of drug product and the function of the respective components are given in Table 1 (investigator’s brochure, page 11).

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

Gene transfer agent delivery method: Intramuscular Injection (IM).

BNT163 drug product is provided as a frozen concentrate for suspension/dispersion to yield the dispersion for injection (the IMP). To prepare the IMP, the drug product is thawed and diluted with isotonic normal saline (0.9% NaCl solution).

Intended target: The intended target is **herpes simplex virus (HSV)-2** and **potentially HSV-1**.

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

Preclinical studies: N/A

Potential for shedding: Pharmacokinetic (PK) and toxicology properties of the RNA-LNP platform were previously characterized using BNT162b2 as a representative vaccine. Additionally, a Good Laboratory Practice (GLP)-compliant repeated dose toxicity study was performed using BNT163 trivalent vaccine, as well as untranslatable control, to test HSV-2 specific antigens and further broaden the RNA-LNP platform toxicology data.

The RNA-LNP remains mainly at the injection site post intramuscular (IM) administration and is only partially distributed to the liver.

Shedding is not a biosafety concern.

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: #13

Research Administrative Actions: #65

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

10. Bates25-302D-1,3

- This registration was prepared by Dr. Sarah Capasso and presented by Mr. Edwin Siu. This registration is for the generation and/or use of genomic sequences to create plasmids for launching recombinant Jamestown canyon and LaCrosse viruses, closely related pathogenic orthobunyaviruses, to analyze requirements for replication. Reassortant and recombinant viruses will be compared to defined strains to map the segments or sequences responsible for the growth differences in mosquito cells. Work will be done in cell culture only. 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.

11. Bomba-Warczak.25-076D-1,3 O-1

- This registration was presented by Ms. Stephanie Adams-Tzivelekidis. This registration is for the generation and/or use of 3rd generation lentiviral vectors with CRISPR/ cas9 technology. The lab is studying mitochondrial long-lived proteins which they identified as residing in mitochondrial cristae of long-lived neurons. The lab will knock-down proteins of interest, such as TFAM and OPA1, as well as tag TFAM with GFP using CRISPR/Cas9 lentiviral technology and will package the virus in HEK 293T, which will be used to infect primary murine neurons. Once primary neurons are infected the lab will carry out pulse-chase experiments with heavy-labelled amino acids (SILAC) to monitor protein turnover rates using mass spectrometry based proteomics. 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.

12. Dowling25-244D-4

- This registration was presented by Ms. Amanda Wong. This registration is for the generation and/or use of transgenic Zebrafish. The lab studies a range of neuromuscular diseases in zebrafish models and will use the established *mtm1* (X-linked myotubular myopathy), *neb* (nemaline myopathy), *ryr1a* and *ryr1b* (Ryanodine receptor type I-related myopathies) and *mtmr5* (Charcot-Marie-Tooth disease) mutant zebrafish lines to in-cross or out-cross with WT fish. The lab will perform comprehensive phenotypic characterization of the zebrafish models and will treat progeny with small molecules or morpholinos/ASOs (captured in IBC 25-240) to test therapies in these transgenic animals. These lines of fish will be imported to Penn and crossed in the Penn Zebrafish facility. 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.

13. iang25-315D-1

- This registration was presented by Ms. Marie- Luise Faber. This registration is for the generation and or use of retroviral vectors. The lab is using amphotropic MESV or MSCV to develop engineer tool cell lines for the analysis of functional readout. These reporters or reporter-like cell lines will be used to measure cell signals in activated immune cells. Vectors expressed with several different fluorescent genes will be transfected into human Jurkat cells to determine T-cell receptors activation levels. The *SrtA*-PDGFR human genes will be transduced into an antigen presenting cell where it will bind biotin to proteins. Containment has been set to BSL-2.
- The registration was discussed by committee members. Dr. Daniel Kessler requested the specific retrovirus name be added into the project description.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved. Pending update to project description.

14. Jurado.....25-322D-1, O-2

- This registration was presented by Ms. Stephanie Adams-Tzivelekidis. This registration is for the generation and/or use of 2nd generation lentiviral vectors expressing mouse syncytin A or syncytin B in 293T (human), MDCK (dog) or Vero (monkey) cell lines. Vectors will be ordered from Addgene and transfected into cells using PolyJet or Lipofectamine. Syncytins are cell-surface proteins which bind their cognate receptors to induce cell-cell fusion, forming multinucleated cell bodies or syncytia. Syncytins are involved in placental development, and the

lab is interested in expressing them in vitro to study whether specific anti-syncytin antibodies can block cell-cell fusion. Containment has been set to BSL-2.

- The registration was discussed by committee members. Dr. Daniel Kessler requested the title be updated to include “Placental development.”
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved pending title update.

15. Haj Dezfulian...25-326D-1,3, O-1

- This registration was presented by Ms. Marie- Luise Faber. This registration is for the generation and/or use of 3rd generation lentiviral vectors. The lab focuses on studying immune stimulation of viruses in human cells. This project uses the Brunello human genome-wide CRISPR knockout sgRNA library in a 3rd generation lenti vector to perform pooled loss-of-function screens in human cells. The genetic material is generated by synthesized chemical synthesis or in vitro transcription from a DNA template. Containment has been set to BSL-2.
- The registration was discussed by committee members. Dr. Daniel Kessler requested the title and project description include the project goal.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved pending updates.

16. Lazar24-264D-1,4 O-1

- This registration was presented by Ms. Stephanie Adams-Tzivelekidis. This registration is for the generation and/or use of 3rd generation lentiviral vectors with CRISPR/Cas9 in NIH-3T3 cells and direct administration into BL6 mice. The lab will use the Lentivirus combined with CRISPR to knock out Nr1d1 and Nr1d2 in NIH-3T3 cells, thereby generating stable knockout cell lines. They will use this cellular model to investigate the impact and mechanism of these genes on regulating circadian rhythms. Lentivirus expressing genes or shRNA will be delivered to mouse livers via hydrodynamic tail vein injection to study the role of NCOR1 and NCOR2, nuclear receptor corepressors, in hepatic metabolism. The lab is investigating those corepressors and their role in diabetes and obesity. The lab intends to use the liver of C57BL/6 wild-type and genetically modified mice to turn off the expression of specific corepressors and associated proteins. 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. Predina25-234D-4, O-2

- This registration was presented by Mr. Edwin Siu. This registration is for the generation and/or use of Lipid Nanoparticle encapsulating nucleic acid. The lab is developing approaches for

stimulating the immune system to more effectively eliminate tumors in mouse models of mesothelioma, lung cancer, and esophageal cancer. In this study they will target these tumors with several different LNPs developed in collaboration with other labs at Penn. The LNP constructs will contain either mRNA or DNA and express one of several intracellular mediators of necroptosis and pyroptosis pathways—potentially inducing immunogenic cell death. LNP injections in mice will allow the lab to observe effects of this treatment on the mouse immune system and tumors. Containment has been set to BSL-1 and ABSL-1.

- The registration was discussed by committee members. Ms. Amanda Wong noted that “No” should be selected on the use of private animals.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved pending correction.

18. Phillips25-269D-4

19. Phillips25-299D-4, O-1

- The registrations were prepared by Dr. Sarah Capasso and presented by Mr. Edwin Siu. Registration 25-269 is for the generation and/or use of mRNA-LNP to deliver therapeutic proteins, including cytokines to mice that have been intracranially xenografted with gliomas. They will also code for proteins commonly mutated in tumors. Registration 25-299 is for the generation and/or use of retroviral vectors to transduce glioma cells to express model antigens as well as for the delivery of CRISPR/Cas9 components to murine T cells, targeting immunomodulatory genes. Both human and murine cells will be used. Vectors will be obtained from Addgene. Cell lines will be obtained from the Human Immunology Core and other collaborators. Containment for 25-269 has been set to BSL-1, ABSL -1 for work with naïve mice and ABSL-2 for mice xenografted with human cell lines. Containment for 25-299 has been set to BSL-2 and ABSL-2.
- The registrations were discussed by committee members. Dr. Daniel Kessler requested that the specific retrovirus be added to the project description.
- Training was complete.
- All members were in favor of approval.
- The IBC registrations pending update to project description.

20. Rader25-164D-4

- This registration was presented by Ms. Marie- Luise Faber. This registration is for the generation and/or use of pcDNA. The lab is studying genes affecting lipid metabolism and cardiovascular disease. ApoC-III and ApoA-V have been shown to modulate Lipoprotein Lipase (LPL) activity, thus affecting triglyceride levels in humans and animal models. Plasmid cDNA encoding WT and variants APOC3 and APOA5 genes will be expressed in human or murine cells. Selected plasmids, using qPCR and Western Blotting, will be injected into mice to induce the transient expression of selected proteins. Containment has been set to BSL-2 and ABSL-1.
- The registration was discussed by committee members.
- Training was not complete.
- All members were in favor of approval.

- The IBC registration was approved pending completion of training.

21. Secreto24-050D-4

- This registration was presented by Ms. Marie- Luise Faber. This registration is for the generation and/or use of modified cells. The Stem Cell and Xenograft Core (SCXC) banks human hematopoietic cells with a full range of xenograft models and services for use by the University of Pennsylvania research community. Core users will provide genetically modified cells for SCXC in-vivo service staff to administer in our immunodeficient mouse, either i.p. or i.m.. The Core is requesting a downgrade for the use of these human cells in their xenograft models. All donated tissue sourced directly from human patients requires testing as described. Tissue testing is conducted by IDEXX BioAnalytics via sterility culture and PCR evaluation for Epstein-Barr virus, Mycoplasma spp, LCMV, Mycobacterium spp., HPV 16, HPV 18, HIV 1, HIV 2, Hep B, Hep C. Upon receipt of test results, SCXC staff enters results into our microbiology database and release mice from isolation. The Core has recently expanded testing panel to include HPV 16, HPV 18, HIV 1, HIV 2, Hep B, Hep C. The Core is asking to pilot this downgrade with Human hematopoietic stem cells (HSCs) procured from commercial sources. Containment has been set to BSL-1, BSL-2, and ABSL-1.
- The registration was discussed by committee members. Ms. Stephanie Adams-Tzivelekidis wanted to confirm that the lab is not culturing the cells after banking. Dr. Secreto confirmed that materials are reputedly sourced from vendors or healthy patients. Ms. Marie- Luise Faber asked if the lab were to add additional cell lines, would the IBC prefer a full review or administrative review. Dr. Daniel Kessler stated this would be at the discretion of the Bio Safety officer.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

22. Weissman.....25-263D-1, 3

- This registration was presented by Ms. Marie- Luise Faber. This registration is for the generation and/or use of 2nd generation lentiviral vectors that display parainfluenza and HIV fusion proteins to be used in neutralization assays. The lab is using a 2nd generation vector because this vector has already been optimized for this type of assay. The vectors are made in the lab via transfection of helper plasmids and will be used with Human Epidermoid carcinoma-2 cells (Hep2 cells) or pulmonary mucoepidermoid carcinoma cells (NCI-H292 cells). Plasmids will also contain fluorescent reporter proteins. 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.

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

23. Wang.....25-316E-3, O-1

- This registration was presented by Mr. Edwin Siu. This registration is for the generation and/or use of guide RNA and CRISPR/ Cas 9. The lab investigates the molecular networks regulating mammalian meiosis and sperm development. They use CRISPR/Cas9 to produce mice with mutations in genes that regulate meiosis to investigate their role in meiosis and to ultimately provide insights into the molecular etiology of infertility in humans. The focus of this study is SKP1, a novel and essential regulator of meiotic double strand break homeostasis, however other genes targeted for mutation will help the lab identify interactions essential to the regulatory role of SKP1. Guide RNA for targeting the genes will be submitted to the PennVet Center for Animal Transgenesis and Germ Cell Research core who will perform the single-cell embryo microinjections to generate the desired mutants. 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

24. Brenner25-317E-1

- This registration was presented by Ms. Amanda Wong. This registration is for the generation and/or use of retroviral vector plasmids with an ecotropic envelope for plasmid delivery of LNPs. The lab aims to evaluate plasmid expression mediated by lipid nanoparticles (LNPs) in different cell lines, comparing the effects of various promoters and reporter proteins exclusively within an LNP-based delivery system. RAW 264.7 cells will be treated with LNPs loaded with the MSCV EF1a-mCHERRY plasmid. Expression levels will be compared against those obtained using a CMV promoter-driven plasmid and an eGFP reporter plasmid. The system is exclusively based on non-viral, LNP-mediated delivery and material is purchased through Addgene. Containment has been set to BSL-1.
- The registration was discussed by committee members.
- Training was complete.
- All members were in favor of approval.
- The IBC registration was approved.

25. Yang.....25-155E-1

- This registration was prepared by Dr. Sarah Capasso and presented by Mr. Edwin Siu. This registration is for the generation and/or use of plasmids to express recombinant proteins in BL21 *E. coli* to study how these regulators function in the cellular protein quality control system. Recombinant proteins will be used in in-vitro assays to examine ligase activity, protein-protein interactions, and substrate handling. Activity will be measured by ubiquitination assays and aggregation prevention tests, with results analyzed by SDS-PAGE, Western blotting, and filter-trap analysis. BL21(DE3) competent cells were purchased commercially from ThermoFisher. Containment has been set to BSL-1.
- 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) Secreto #24-050 Downgrade [registration #21 above & attachments] (Marie-Luise)
- (4) HSC-ABSL2-downgrade-10-6-25.
 - (5) SCXC-ABSL2-downgrade-proposal

- The downgrade request was evaluated and discussed by committee members as part of registration review for #24-050.
- Details of downgrade approval appear above in comments for #24-050.
- This downgrade request was approved.

- (b) 2026 IBC Meeting Schedule [*draft*]. (Amanda)

- A draft of the IBC meeting schedule for 2026 was presented, IBC members are asked to review and provide feedback, noting any comments or concerns.

4. Old Business:

- (a) No Old Business Scheduled.

5. End Meeting:

- The Institutional Biosafety Committee was adjourned by Dr. Daniel Kessler at **11:13 AM**.

Our next meeting scheduled for Monday, November 24th, 2025, will be held on site at the EHRS Office with a Teleconference option, at 10:00 am. A light Brunch will be provided.