RUSH

RUSH Institutional Biosafety Committee (IBC)	
Meeting Date	July 30, 2025
Meeting Time	12:00 PM – 1:00 PM
Meeting Type	Virtual via Microsoft Teams
IBC Members Present	1. Amarjit Virdi, Ph.D. (IBC Chair) 2. Ed R. Blazek, Ph.D., SM (NRCM) (BSO) 3. James Bremer, Ph.D. (IBC Member / Virology) 4. Jeffrey Oswald, D.V.M., Comparative Research Center (IBC Member / Veterinary Medicine) 5. Liudmila Romanova, Ph.D. (IBC Member / Expertise Neurological Sciences) 6. Adam Roubitchek, Ed.D. (Local Non-Affiliated Member) 7. Jennifer Strong (*ex officio* Non-Voting / Research Compliance) 8. Brett Williams, M.D. (IBC Member / Infectious Disease Physician)
Quorum	Quorum was declared by the Chair. The IBC has nine voting members, and five members are required to conduct business.
Other Individuals in Attendance	1. Christine VanTubbergen, MPH (Program Manager, Office of Research Affairs) 2. Rebecca 'Bex' Ober, D.V.M. (Senior Director, Comparative Research Center)
Call to Order	The IBC Chair called the meeting to order at 12:00 PM.
Conflicts of Interest	The IBC Chair reminded all members present to identify any conflicts of interest as each application is reviewed.
Review and Approval of Previous Meeting Minutes	June 18, 2025 Motion: Approve the minutes as circulated. Votes: 7-0-0-0 (for-against-abstain-recuse)

Review of Prior Business		
PI Name & ORA #	**Application**	**Approval Date**
Sunita Nathan, M.D. 20050801-IBC33	Continuing Review 05	7/28/25
João Mamede, Ph.D. 22071201-IBC01	New Application	7/24/25
Mouhammed Kelta, M.D. 23081106-IBC06	Amendment 05	7/22/25
Sunita Nathan, M.D. 21060306-IBC23	Amendment 20	7/17/25
Elizabeth Berry-Kravis, M.D. 24090903-IBC04	Amendment 03	7/16/25
Sunita Nathan, M.D. 20050801-IBC32	Amendment 36	7/15/25
Sunita Nathan, M.D. 19070910-IBC20	Amendment 19	7/15/25
Sunita Nathan, M.D. 24061205-IBC04	Amendment 03	7/15/25
Elizabeth Berry-Kravis, M.D. 23092006-IBC15	Amendment 13	7/10/25
Sunita Nathan, M.D. 21070206-IBC20	Continuing Review 04	7/9/25
Mouhammed Kelta, M.D. 24082607-IBC04	Amendment 04	7/9/25

Elizabeth Berry-Kravis, M.D. 24022207-IBC05	Continuing Review 01	7/9/25
Thomas Westbrook, M.D. 24032202-IBC03	Amendment 02	7/9/25
Neepa Patel, M.D. 23091102-IBC02	Amendment 01	7/7/25
Elizabeth Berry-Kravis, M.D. 24042305-IBC09	Continuing Review 01	6/25/25
Sunita Nathan, M.D. 20050801-IBC31	Amendment 35	6/25/25
Sunita Nathan, M.D. 21070206-IBC19	Amendment 13	6/25/25
Sunita Nathan, M.D. 24061205-IBC03	Amendment 02	6/20/25

New IBC Applications for Review	
PI Name	Deborah Hall, M.D.
ORA#	24072503-IBC01
Project Overview	**III-C-1** This is a first-in-human, open-label, multi-center, dose escalation Phase 1/2 clinical trial designed to assess the safety, tolerability, and efficacy of a single intravenous (IV) dose of CAP-003 administered to adult patients with Parkinson's Disease associated with glucocerebrosidase beta 1 (*GBA1*) mutations. CAP-003 is a novel gene therapy consisting of an engineered capsid capable of crossing the blood-brain barrier and is designed to supplement the β-glucocerebrosidase (GCase) enzyme, which is a lysosomal hydrolase and is affected by *GBA* mutations. CAP-003 is designed to target delivery of a functional copy of the *GBA1* gene to nerve cells while minimizing off-target tissue effects. The goal of CAP-003 is to restore normal GCase activity and slow the progression of disease. This trial is sponsored by Capsida Biotherapeutics, Inc. (ClinicalTrials.gov ID: NCT07011771). The capsid of CAP-003 is derived from adeno-associated virus (AAV). There is preclinical data for CAP-003 in non-human primates (NHPs). In NHPs, CAP-003 shows evidence of exceeding the threshold for normalizing GCase activity and exceeding the threshold of GCase activity needed to overcome the expected deficient in patients. Compared to intra-cisterna magna (ICM) delivery of AAV9, there is evidence that CAP-003 leads to increased GCase protein levels in the brain and that CAP-003 targets nerve cells. Compared to IV-delivered AAV9, there is evidence that there is reduced biodistribution of CAP-003 in the liver and dorsal root ganglia (DRGs). GCase activity in the brain of NHPs treated with CAP-003 was positively correlated with GCase protein levels in the cerebrospinal fluid (CSF). Participants in this trial will receive a single IV infusion of CAP-003 and then be followed for 2 years. Participants in Phase 1 will be dosed sequentially. Phase 2 will allow for participants to be dosed concurrently, if safety and tolerability data from Phase 1 are determined to be acceptable.
NIH Guidelines Section	**III-C-1**
Risk Assessment & Discussion	• Adeno-associated virus is a RG-1 agent. • The novel vector in CAP-003 is replication deficient.

	• Syringes and IV bags will be prepared in a BSL-2 biosafety cabinet (BSC). • PPE consisting of lab coat, gloves, rear-closing gown, surgical mask, and eye protection will be utilized when preparing or administering the agent. • Non-sharps materials that come into contact with the agent will be disposed of as biohazardous waste. • Risks to participants described in the informed consent form (ICF) should be made to be consistent with those of other, related gene therapies.
Training	For research requiring IBC oversight, the PI must complete the CITI Initial Biosafety Training course and clinical lab personnel must complete the CITI Basic Biosafety Training course. For research involving human gene transfer, the PI and personnel must complete either the CITI Recombinant Clinical Biosafety Course or the CITI Recombinant Clinical Coordinator course, depending on research activity involvement. At least one individual has current CITI International Air and Transportation Association (IATA) training.
Occupational Health Representative Review (if applicable)	Not applicable.
BSL Assignment	• BSL-1 for preparation and administration of the agent.

IBC Vote	• A motion was made to provisionally approve this application pending the following conditions be met:
	  • Modify the ICF to state that while CAP-003 has never been used to treat humans, other related forms of AAV vectors have occasionally caused systemic effects and could potentially result in death
	  • Description of waste disposal methods for sharps
	  • Addition of a pharmacist to study personnel
	  • Addition of BSC location and up-to-date certification
	Votes:
	• 7-0-0-0
	Conflicts of Interest: None

New IBC Applications for Review	
PI Name	Elizabeth Berry-Kravis, M.D.
ORA#	21070805-IBC01
Project Overview	**III-C-1** This is a first-in-human, multi-center Phase 1/2 clinical trial designed to assess the safety, tolerability, and efficacy of MZ-1866 administered via intracerebroventricular (ICV) injection to adult and pediatric patients with Pitt Hopkins Syndrome (PTHS). Patients with PTHS have mutations in the Transcription Factor 4 (*TCF4*) gene, which encodes for the TCF4 protein. MZ-1866 is a recombinant AAV9 gene therapy designed to deliver a functional copy of the *TCF4* gene to cells. This trial is sponsored by Mahzi Therapeutics, Inc. Participants in this trial will receive a single injection of MZ-1866.
NIH Guidelines Section	**III-C-1**
Risk Assessment & Discussion	• Adeno-associated virus is a RG-1 agent. • The novel vector in MZ-1866 is replication deficient. • Agent will be prepared in a BSC.

	• All materials used for infusion will be disposed of as biohazardous waste. • PPE consisting of gloves, rear-closing gown, surgical mask, and eye protection will be utilized when preparing or administering the agent. • Risks to participants described in the ICF are appropriate and consistent with those for other, related gene therapies.
Training	For research requiring IBC oversight, the PI must complete the CITI Initial Biosafety Training course and clinical lab personnel must complete the CITI Basic Biosafety Training course. For research involving human gene transfer, the PI and personnel must complete either the CITI Recombinant Clinical Biosafety Course or the CITI Recombinant Clinical Coordinator course, depending on research activity involvement. At least one individual has current CITI International Air and Transportation Association (IATA) training.
Occupational Health Representative Review (if applicable)	Not applicable.
BSL Assignment	• BSL-1

IBC Vote	• A motion was made to provisionally approve this application pending the following conditions be met:
	  • Name of the neurosurgeon performing the procedure, and if the surgeon is located at Rush, then they should be added to the project's personnel
	  • Addition of the location where the surgery will be performed
	  • Submission of current BSC certifications
	<u>Votes</u>:
	• 7-0-0-0
	Conflicts of Interest: None

New IBC Applications for Review	
PI Name	Elizabeth Berry-Kravis, M.D.
ORA#	25032404-IBC01
Project Overview	**III-C-1** This is a first-in-human, multi-center Phase 1/2 clinical trial designed to assess the safety, tolerability, and efficacy of MVX-220 administered via intra-cisterna magna (ICM) injection to adult and pediatric patients with Angelman Syndrome (AS). Patients with AS have missing or non-functional copies of the *UBE3A* gene, which encodes for the UBE3A protein. MVX-220 is a novel hu68AAV gene therapy designed to deliver a functional copy of the *UBE3A* gene to neurons. This trial is sponsored by MavriX Bio LLC. There is preclinical data for MVX-220, which provides evidence that administration of MVX-220 restores UBE3A protein expression and ameliorates symptoms in a mouse model of AS. Participants in this trial will receive a single injection of MVX-220.
NIH Guidelines Section	**III-C-1**
Risk Assessment & Discussion	• Adeno-associated virus is a RG-1 agent. • The novel vector in MVX-220 is replication deficient. • Agent will be prepared in a BSC.

	• All materials used for infusion will be disposed of as biohazardous waste. • PPE consisting of gloves, rear-closing gown, surgical mask, and eye protection will be utilized when preparing or administering the agent. • Risks to participants described in the ICF are appropriate and consistent with those for other, related gene therapies.
Training	For research requiring IBC oversight, the PI must complete the CITI Initial Biosafety Training course and clinical lab personnel must complete the CITI Basic Biosafety Training course. For research involving human gene transfer, the PI and personnel must complete either the CITI Recombinant Clinical Biosafety Course or the CITI Recombinant Clinical Coordinator course, depending on research activity involvement. At least one individual has current CITI International Air and Transportation Association (IATA) training.
Occupational Health Representative Review (if applicable)	Not applicable.
BSL Assignment	• BSL-1

IBC Vote	• A motion was made to provisionally approve this application pending the following conditions be met:
	  • Name(s) of the physician performing the injection
	  • Submission of current BSC certifications
	Votes:
	• 7-0-0-0
	Conflicts of Interest: None

New Business	Nothing to report.
Review of Incidents	• Information regarding one serious adverse event and three adverse events for study 19010804 (ClinicalTrials.gov ID: NCT04120493) was previously submitted by the study team for review by the IBC Sub-Committee. The IBC Sub-Committee's review concluded that the adverse events did not warrant an amendment.
Inspections/Ongoing Oversight	Nothing to report.
IBC Training	Members were educated on the new process for study teams to submit safety and adverse event information or reports to the Committee.
Public Comments	There were no public comments.
Adjournment	The IBC Chair moved to adjourn the meeting at 1:00 PM The next meeting scheduled is for August 20, 2025 at 12:00 PM via Microsoft Teams.