**Minutes**

**Institutional Review Board - Institutional Biosafety Committee for**

**Human Subjects Meeting - IBC**

**August 15, 2025**

**Location:** Virtual

**Total Voting Members 10; Quorum 6**

**Members Present:** Ana Nobis, MD, MPH (PS), Antonios Hatzopoulos, PhD (OS), Bipin Savani, M.D. (PS),

Cary Fu, M.D. (PS), Donna Torr, PharmD (OS), Douglas Johnson, M.D., MSCI (PS), Kimberly Towers, BS

(NS), Richard DiTullio, PhD (OS), Rolinda Bailey, BSMT(ASCP) (NS)

**Members Absent:** Allison Wheeler, M.D., MSCI (PS)

**Ex-Officio Members Present:** None

**Administrative Staff Present:** James Arrington, BA, CIP, Tiffany Alexander, MPH, BSN, RN, CIP

**Guests: D.** Christopher Aiken; Dr. Jennifer Gaddy - both joining the IBC-HS Committee. Present today for their meeting observation.

**Meeting Called to Order:** 8:32AM

**Meeting Adjourned:** 9:21AM

**Announcements and Education**

Happy August; new Committee member observations today! Reminder on Annual Training and

Evals/Feedback Forms via Redcap; AAHRPP Site Visit in two weeks; NIH new Minutes Guidelines now in effect, set from June will be posted publicly.

**Reveal Possible Conflicts of Interest**

None

**Review and Approval of the Previous Minutes and Review of Approvals by the Chair**

The Chair polled the committee for corrections to the minutes for the meeting dated 6/06/2025. No changes were provided. The minutes were approved as written. The approval of these minutes will be the first to be provided on the public website to meet NIH guidelines.

**Subcommittee**

**IRB#: 250868**

**VICCPHI 24512 (A2B694-101) A Seamless Phase 1/2 Study to Evaluate the Safety and Efficacy of**

**A2B694, an Autologous Logic-gated Tmod™ CAR T, in Heterozygous HLA-A\*02 Adults With Recurrent**

**Unresectable, Locally Advanced, or Metastatic Solid Tumors That Express MSLN and Have Lost HLA-**

**A\*02 Expression**

**PI: Cathy Eng, MD**

**Sponsor:** A2 Biotherapeutics, Inc.

**Summary:** The purpose of this study is to test this experimental therapy using modified immune cells (called A2B694). Before patients receive A2B694, they will receive treatment with a combination of 2 drugs, cyclophosphamide and fludarabine, that are already used regularly for lymphodepletion.

**Subcommittee:**

**Comments:**

The Reviewers presented a summary and comments followed by discussion. A Reviewer stated this is an

Autologous Logic-Gated Tmod™ Cells Transduced with a Single Lentiviral Vector Expressing a MSLNTargeted CAR Activator and an HLA-A\*02-Targeted Blocker for the Treatment of Solid Tumors. The Sponsor for the study is A2 Biotherapeutics, Inc. The Vanderbilt University Medical Center Principal Investigator isCathy Eng, MD, Division of Hematology/Oncology. The Investigational Product being used in the study is IMP: A2B694. All current key study personnel have completed the required human subjects training requirements to conduct the study.

A Reviewer stated this is a, seamless Phase 1/2, multicenter, open-label, non-randomized study. Adults that are germline heterozygous for HLA-A\*02 with recurrent, unresectable, locally advanced, or metastatic colorectal cancer, non-small cell lung cancer, pancreatic cancer, ovarian cancer, mesothelioma, or other solid tumors that express MSLN and have lost HLA-A\*02 expression.

A2B694 is an autologous CAR T-cell product genetically modified to express a MSLN specific T-cell activating receptor alongside a blocker receptor specific for HLA-A\*02. Monitoring for T-cell clonal outgrowth will be performed at multiple time points in the study. Participants will be screened at multiple timepoints.

This study consists of Phase 1 dose-escalation and dose-expansion portions and a Phase 2 cohort-expansion portion. Loss of Heterozygosity (LOH) occurs when a heterozygous genetic locus loses one of its two parental alleles. LOH is commonly observed in solid tumor malignancies.

As the populations for this study have few or no curative options, and standard therapies present their own toxicity and risk profiles, the benefit-risk ratio for this study is acceptable. .No additional biosafety concern noted. The Reviewers noted acceptance of the informed consent documents with no issues.

There were no specific comments for discussion from the Pharmacy Reviewer. The Occupational Health

Reviewer noted a recent change in the Occupational Health Clinic Hours for the Test Article Hazard Profile Form. This will be updated administratively. There were no comments for discussion from the Community Members.

The Committee agreed all items have been addressed and recommended approval under BSL-2 conditions.

**Motion:** The Committee found that the description of the agent, use, precautions, and risks are appropriately described in the submitted documents including the consent document(s). The Committee found that the requirements for protocol submission, review, and reporting per Section III-C and section III-C-1 NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules have been met. Approval was recommended.

**Total votes for Approve: 9** (Total Members Voting: 9)

**For: 9 Against: 0 Abstained: 0 Abstained:**

**Quorum Notes**