Application #	CLIN1-13985 #2
Title (as written by the applicant)	Development of an Engineered Autologous Leukemia Vaccine for Stimulating Cytolytic Immune Responses to Residual Leukemic Stem Cells
Therapeutic Candidate (as written by the applicant)	Our proposed autologous acute myelogenous leukemia (AML) vaccine designed to stimulate induction of anti-leukemic cytolytic activity and improve relapse free survival (RFS).
Indication (as written by the applicant)	Older leukemia patients who achieve remission with chemotherapy and are at high risk of relapse, but are not eligible for allogeneic transplantation
Unmet Medical Need (as written by the applicant)	Most patients with acute myelogenous leukemia (AML) are over 60 years old. Despite chemotherapy, patients usually relapse. Although allogeneic transplantation improves outcomes, many older patients are ineligible due to co-morbidities. Thus, there is an unmet need for safe and effective treatments to improve relapse-free survival
Major Proposed Activities (as written by the applicant)	• Generate three clinical scale vaccine batches meeting release criteria and complete safety studies including RCL testing and growth inhibition assays • Toxicology studies by serial vaccination of mice with murine version of the proposed therapeutic, potential drug product hazard study in immune deficient mice, • Obtain clinical lentivirus prep with titer, identity, sterility, etc. assays completed, • File IND with trial design; begin clinical start-up activities
Funds Requested	$6,000,000
GWG Recommendation	Tier 1: warrants funding
Process Vote	All GWG members unanimously affirmed that “The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG.” Patient advocate members unanimously affirmed that “The review was carried out in a fair manner and was free from undue bias.”

SCORING DATA

Final Score: 1

Up to 15 scientific members of the GWG score each application. The final score for an application is the average of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	1
Count	15
Votes for Tier 1	15
Votes for Tier 2	0
Votes for Tier 3	0

- A score of “1” means that the application has exceptional merit and warrants funding
- A score of “2” means that the application needs improvement and does not warrant funding at this time but could be resubmitted to address areas for improvement
- A score of “3” means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review for at least six months after the date of the GWG’s recommendation

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel’s discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

GWG Votes	Does the project hold the necessary significance and potential for impact?
Yes: 14	• The proposal seeks to develop an immune based strategy to control minimal residual disease and relapse in acute myelogenous leukemia (AML). The agent has the potential to improve outcomes in this disease. • Yes. In particular, the proposed therapy is potentially a less toxic therapeutic option for older patients with poorer performance status. • AML relapse after hematopoietic stem cell transplantation represents an unmet medical need. The proposed product is aimed at prophylaxis of AML relapses after the first line of therapy. • In response to feedback from the prior review, the applicant discusses the competitive landscape and provides an overview of previous efforts to use cancer vaccines in AML.
No: 0	*none*
GWG Votes	**Is the rationale sound?**
Yes: 14	• The rationale is sound based on the available data. • The preclinical data as well as learnings and considerations from previous vaccine clinical studies support continued clinical development. • The scientific rationale is sound. Preliminary studies support further development. • In response to the prior review, the authors acknowledge a relatively high probability of manufacturing failure and provide risk mitigation strategies.
No: 0	*none*
GWG Votes	**Is the project well planned and designed?**
Yes: 14	• I appreciate their responsiveness to the prior review comments. They removed the bone marrow microenvironment study and clarified the questions around manufacturing. • The investigators have adequately addressed the issues raised in the previous submission. • The applicant has been thoroughly responsive to concerns highlighted in the initial review, providing carefully detailed clarifications and additional assessments to both preclinical and clinical proposed studies. • The manufacturing plan has been updated including transfer of bone marrow aspirates to a FACT-accredited BMT/Cell Research Lab for processing. • The manufacturing plan is appropriately designed. Potential risks and mitigation strategies are discussed. • Major activity #4 was removed as a response to the prior review.
No: 0	*none*
GWG Votes	**Is the project feasible?**
Yes: 14	• The investigators present a logical set of preclinical studies as well as development of the clinical agent. • Additional team members have been added to support the proposal. • The timeline looks reasonable. The proposed studies look feasible. • The team is appropriately qualified and has an access to all needed resources. • There have been a few minor alterations to the manufacturing summary.
No: 0	*none*
GWG Votes	**Does the project uphold principles of Diversity, Equity, and Inclusion (DEI)?**
Yes: 14	• Alternatives to HSCT are critical for minorities, as was discussed. • Very well - no additional concerns. • DEI principles are reflected in the application.
No: 0	*none*

DIVERSITY, EQUITY, AND INCLUSION IN RESEARCH

Following the panel's discussion of the application, the patient advocate and nurse members of the GWG were asked to indicate whether the application addressed diversity, equity and inclusion, and to provide brief comments. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

DEI Score: 9.0

Up to 7 patient advocate and nurse members of the GWG score each application. The final score for an application is the median of the individual member scores. Additional parameters related to the score are shown below.

Score	Patient Advocate & Nurse Votes	Does the project uphold principles of Diversity, Equity, and Inclusion (DEI)?
9-10: Outstanding response	5	• Strong DEI components. • Very strong awareness and focus on financial needs, tracking of enrollees, demonstrated capabilities from the institution on outreach and interactions with patients.
6-8: Responsive	1	*none*
3-5: Not fully responsive	0	*none*
0-2: Not responsive	0	*none*