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March 17, 2026
Open Letter to the Application Review Subcommittee

Re: CLIN2-19191 – TriLeukeVax (TLV): A first in human trial of an engineered autologous vaccine to enhance relapse free survival in AML patients. (Karin M.L. Gaensler, P.I.)

Dear Members of the Application Review Subcommittee,

We thank the Grants Working Group for their thoughtful evaluation and are grateful for their recognition of the many strengths of our program. We appreciate the Reviewers' careful assessment and suggestions and welcome the opportunity for the TLV program to be considered by the ARS within the broader context of CIRM's mission to advance regenerative medicine therapies that address serious unmet medical needs and deliver benefit to Californians. We include:

1) An Executive summary of the goals and accomplishments of the TLV program.
2) P.I. letter to the ARS outlining the TLV program and the urgent medical needs of transplant ineligible AML patients, individuals with a rare disease who are relapsing and losing their lives, with no new options available.
3) GWG comments highlighting the strengths of our Value Proposition, Rationale, Project plan, and the Population impact of our goal to enhance TLV affordability/access in community practices in California.

Executive Summary

- AML remains a devastating disease. TriLeukeVax, our engineered autologous vaccine, was developed to address the urgent unmet need for therapies to reduce relapse and increase survival in transplant-ineligible patients.
- Development of the TLV treatment strategy was intentionally designed to enable broad patient access across California and to fill this unmet need.
- TriLeukeVax Phase 1 funding would broaden the scope of CIRM's hematologic oncology program portfolio.
- The TLV program reflects a sustained translational effort spanning nearly a decade, including funding from CIRM at each stage of development (TRAN 1, CLIN 1).
- Funding now is critical to enable initiation of our trial-ready TLV program with both Fast-Track and Orphan Drug designations.
- This is a first-in-human evaluation of post-remission serial TLV vaccination in AML patients following frontline Azacitidine/Venetoclax (aza/ven) therapy.
- TLV vaccines will be administered during the post-remission period following aza/ven induction therapy.
- Importantly, the approach of engineering tumor cells to express the immunostimulatory combination of CD80 and IL-15IL-15Ra to generate other tumor cell vaccines could be readily be assessed. In addition, given the challenges stimulating immunity in older patients, we will pursue approaches for enhancing vaccine potency by combining TLV with other drugs or immunostimulatory strategies.
- Engineering studies conducted in the UCLA Kohn laboratory have demonstrated the feasibility of manufacturing TLV from cryopreserved AML patient bone marrow samples with consistent transduction efficiency and product release characteristics.
- We are ready to enroll patients now. The protocol has had broad institutional scientific review and has been approved by the Cancer Immunotherapy Site Committee and the Protocol Review and Monitoring Committee of the UCSF Helen Diller Family Comprehensive Cancer Center.
- The team has assembled a Strategic Planning Committee (SPC) that "brings both business and scientific acumen and clinical, medical, manufacturing and analytical staff appropriate expertise to complete the phase 1" (Reviewer's comments). Our SPC will play an integral role in partnering with a CDMO, and planning BLA sponsorship, potency assay development, and regulatory strategy.
- The TLV AML vaccine program is a California-based, CIRM-supported translational pipeline. It is now poised for clinical evaluation as an urgently needed option for an orphan population with no approved immunotherapeutic options to maintain their remission status and increase survival.

P.I. Karin M.L. Gaensler Letter to ARS:

AML remains a devastating disease, particularly for older patients who are not candidates for intensive chemotherapy or allogeneic stem cell transplantation (HSCT). Frontline regimens such as aza/ven can induce remission in 50-60% of patients, but relapse is common and survival after disease progression is poor. For this population—many of whom are treated outside major transplant centers—there are no approved therapies specifically designed to reduce/prevent relapse and increase survival, once remission has been achieved.

Development of the TLV treatment strategy was intentionally designed to enable broad AML patient access across California and to fill this unmet need. Manufacturing will occur centrally at the UCLA Center for Advanced Biotherapies, a CIRM funded GMP facility supporting advanced cell therapy production. Once remission is documented, TLV could be shipped as a cryopreserved serially administered post-remission vaccine to community clinical sites, thawed, irradiated in any health care facility with a blood bank irradiator, and administered subcutaneously using standard nursing procedures. TLV will be serially administered during the post-remission period. Endpoints including relapse free survival, overall survival, and safety and feasibility will be the basis for moving forward ("go/no go"). By enabling treatment beyond specialized transplant centers and integrating community-based oncology networks, the TLV program aligns closely with CIRM's commitment to reduce costs and ensure that regenerative medicine innovations are accessible to diverse patient populations throughout California.

TLV was developed to address this urgent unmet need for therapies to reduce relapse. TLV is designed to stimulate durable anti-leukemic responses in the patients' own immune cells that then can eliminate the residual leukemic blasts and stem cells that drive recurrence. The strategy draws on the well-established graft-versus-leukemia effect of donor immune cells observed following HSCT. To reproduce this active immune surveillance, administration of the personalized autologous vaccine (TLV) is used to stimulate host immunity without the toxicity, donor dependence, or accessibility issues associated with HSCT.

We have been successful in achieving important regulatory milestones. The U.S. FDA cleared our Investigational New Drug (IND) application 31747 (6/25/25). FDA Fast Track designation was awarded (10/29/25) and FDA Orphan Drug designation (1/13/26), recognizing both the urgent need in AML relapse prevention and the potential of TLV to address it. The TLV platform is further supported by established intellectual property, including 2 issued patents (U.S. Patent Nos. 12,186,342-B2 and 12,453,763-B2), and incorporates immune-stimulatory components authorized through collaboration with the NCI.

Funding of the TLV platform would expand an important dimension of CIRM's hematologic oncology programs from a portfolio perspective. CIRM has previously invested in transformative approaches including CAR-T cell therapies, gene-modified hematopoietic stem cell therapies, and transplant tolerance approaches. TLV addresses a major gap in therapeutic strategies for leukemia by targeting minimal residual disease after remission induction. As such, TLV complements existing programs by introducing a relapse-prevention strategy not represented within the current CIRM clinical portfolio.

We deeply appreciate the input of the Reviewers and will incorporate their suggestions as we begin studies to generate the safety, feasibility, and translational data required to guide TLV development and inform future trials.

In summary, the TLV AML vaccine program represents a California-based, CIRM-supported translational pipeline that has progressed from early discovery through regulatory clearance. By targeting leukemic blasts and stem cells responsible for relapse, TLV provides a novel immunotherapeutic strategy, and the opportunity to expand the range of regenerative medicine approaches available to patients with AML. Advancing this program is a critical, time-sensitive opportunity to enable CIRM support of this first-in-human evaluation of TLV while building on prior CIRM investments and enabling potential benefit for patients across California.

Every AML patient desperately hopes for new therapeutic options that address the specter of relapse.

We thank you for your consideration of this much needed and ready to be implemented clinical program.

Sincerely,

Karin L Gaensler M.D.

Strengths of the TLV Program noted by the GWG

- "The autologous approach serves a population with limited options for staying in remission (there are no approved immunotherapies). It leverages known post-HSCT biology for …MRD eradication."
- "Well-outlined value proposition - Increasing patient access through engagement of oncology community clinics - Solid rationale, and convincing preliminary data."

Value Proposition

- "There is…. a strong case for the benefit for an autologous vaccine that could prevent relapse. HSCT ineligible patients also experience more frequent relapse due to persistence of minimal residual disease (MRD) and the absence of leukemia-specific immune surveillance."
- "Compelling need to serve a rare, orphan patient population with no approved immunotherapy,
  -a very plausible mechanism of action - realistic possibility of prolonged remission, extended progression free survival / overall survival, improved patient quality of life, and reduced caregiver burden."
- "The value proposition for the healthcare systems is mostly two-fold: 1) pharmacoeconomic impact by preventing relapses and (2) administration in the outpatient settings in oncology community clinics. Both are significant cost-saving strategies."

Rationale

- "The candidate AML vaccine is transduced autologous AML cells that co-express proteins that activate leukemia-specific cytotoxic T cells to mimic graft versus leukemia (GvL), which is well-known biology for disease eradication after allo HSCT….. added to Azacytidine/Venetoclax low intensity conditioning, the vaccine candidate should be effective against MRD."
- Co-culture of post-remission AML patient T cells with the vaccine candidate … induced robust, leukemia-specific cytolytic responses."
- "Engineering runs ……established GMP manufacturing feasibility.

Project Plan and Design

- "The use of a rapid dose-escalation scheme with a 3+3 design as a backup is reasonable, given that the agent is unlikely to cause meaningful toxicity based on other clinical autologous vaccine studies…The contingency plans are reasonable."
  Project Team and Resources (Team was favorably reviewed).
- "The Strategic Planning Committee brings both business and scientific acumen and clinical, medical, manufacturing, and analytical staff appropriate expertise to complete the phase 1."

Population Impact:

- "Estimates suggest 2500 patients/yr in California with 450-480 patients/yr eligible for therapy
  The economic burden of relapsed/refractory (R/R) AML is substantial……. the candidate could improve ..outcomes...in a target population often excluded from intensive or novel treatments."
- Outpatient administration supports the feasibility of community-based vaccine delivery programs……. standard of care has failed to deliver durable disease control, resulting in frequent relapses, hospitalization, and high end-of-life care costs. This approach seeks to shift this paradigm by inducing broad, patient specific immune responses capable of long-term disease control, without restrictions on AML subtype, donor identification, or HLA matching."