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Open Letter to the Application Review Subcommittee
Re: CLIN2-19191 – TriLeukeVax (TLV)

Dear Members of the Application Review Subcommittee,

I am writing in support of the TriLeukeVax (TLV) for acute myelogenous leukemia (AML) CLIN2 proposal led by Dr. Karin Gaensler at the University of California, San Francisco. My perspective on this program comes primarily from the standpoint of translational development and manufacturing of advanced cellular therapies.

Over the past three decades, my laboratory and clinical teams have worked to translate hematopoietic stem cell gene therapies from early laboratory discoveries to first-in-human clinical trials and ultimately to regulatory approval. These experiences have underscored that the most significant challenges in bringing novel cellular therapies to patients are often not related to scientific rationale but to the practical realities of manufacturing, regulatory development, and safe clinical implementation.

In this regard, one of the most compelling aspects of the TLV program is the careful attention that has been given to its translational development pathway. The program has progressed through multiple stages of preclinical and manufacturing development supported in part by prior CIRM funding, culminating in clearance of IND 31747 by the U.S. Food and Drug Administration. Achieving IND clearance for a complex autologous cellular product reflects substantial progress in product characterization, manufacturing development, and regulatory engagement.

My laboratory at UCLA has been directly involved in evaluating manufacturing feasibility for the TLV platform. These studies demonstrated that autologous AML cells collected at diagnosis can be successfully engineered using lentiviral transduction to express the immunostimulatory components required for TLV activity while maintaining acceptable product viability, transduction efficiency, and release characteristics. Importantly, these studies confirmed that manufacturing can be performed reliably using cryopreserved patient samples, enabling coordination between diagnostic cell collection, centralized manufacturing, and later clinical administration.

The clinical product for this study will be manufactured at the UCLA Center for Advanced Biotherapies (CAB), a CIRM-funded GMP facility with extensive experience producing gene-modified and cellular therapy products for early-phase clinical trials. The CAB facility was established specifically to support the translation of innovative academic discoveries into clinical testing and represents an important component of the state's regenerative medicine manufacturing infrastructure.

From a translational standpoint, the TLV manufacturing strategy is practical and well aligned with the needs of an early-phase clinical study. Centralized manufacturing at a GMP facility, followed by cryopreservation and distribution of the final product for administration, is a model that has been successfully used in numerous cell therapy programs. The investigators have also incorporated appropriate quality systems, product characterization, and chain-of-custody procedures necessary for safe clinical implementation.

Equally important, the clinical trial will be conducted at UCSF within the CIRM Alpha Stem Cell Clinic network, an environment specifically designed to support early-phase regenerative medicine studies requiring specialized cell handling and monitoring capabilities. The integration of discovery and translational science at UCSF with GMP manufacturing at UCLA reflects the collaborative infrastructure that California voters approved and that CIRM has developed to accelerate the translation of innovative cell and gene therapies.

Based on my experience developing and implementing complex cellular therapies in the clinic, I believe the TLV program has appropriately addressed the major translational challenges in manufacturing and delivering an autologous cellular product. The development pathway, regulatory preparation, and manufacturing strategy provide a strong foundation for safe and effective execution of the proposed Phase 1 study.

For these reasons, I believe the TLV program represents a scientifically credible and translationally feasible opportunity to evaluate a novel immunotherapy strategy to prevent relapse in AML. Continued support through the CLIN2 program would allow this California-based collaboration to move forward with clinical testing of an innovative approach that could ultimately expand therapeutic options for patients with this serious disease.

Thank you for your consideration.

Sincerely,

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