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March 16, 2026

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

Dear Members of the Application Review Subcommittee,

I am writing to offer my perspective on the regulatory readiness and development strategy for the TriLeukeVax (TLV) clinical program proposed by Dr. Karin Gaensler and colleagues at the University of California, San Francisco. Having worked extensively in regulatory science and product development across both government and translational research environments, I have had the opportunity to review the overall development strategy for this program and its progression toward early clinical evaluation.

The TLV program has advanced through a structured translational pathway that includes preclinical development, IND-enabling activities supported by the California Institute for Regenerative Medicine, and successful regulatory engagement with the U.S. Food and Drug Administration. Clearance of IND 31747, along with the grant of Fast Track designation on October 29, 2025, and Orphan Drug designation in January 2026, reflect significant regulatory progress and support the feasibility of advancing this platform into clinical testing. Collectively, these milestones strengthen the program's potential path toward clinical development and eventual commercialization.

From a regulatory and development perspective, the proposed Phase 1 study is an appropriate next step in the clinical evaluation of this therapy. In addition to evaluating safety, feasibility, and preliminary biological activity, the Phase 1 study is intended to generate the translational and analytical data needed to support subsequent development. Consistent with the overall development plan, risks further down the pipeline are being addressed in part through the early development of potency and efficacy assays to inform Phase 2 trial design. Given the program's Fast Track designation, the team anticipates obtaining feedback and early alignment with FDA in interactions during and following Phase 1, on potency assay development, product characterization, and other CMC elements needed to support efficient progression into later-stage studies. This approach enables early alignment with FDA on potency strategy and CMC readiness.

The Phase 1 study is designed to establish safety, feasibility, and preliminary biological activity and generate the data necessary to guide subsequent clinical development. This type of carefully staged early-phase investigation is essential for translating promising cellular and immune-based therapies into clinically actionable treatment strategies.

Fast Track supports acceleration of the development and submission process, as was noted by the Reviewers. While a precise BLA submission and approval date cannot yet be confirmed at the Phase 1 stage, Fast Track designation provides an opportunity for more frequent FDA engagement and potential rolling review, which can support a more efficient path to licensure. And if granted Priority Review, the FDA's current review goal for an original BLA is 6 months from the 60-day filing date.

Programs such as TLV illustrate the importance of integrating scientific innovation with a disciplined regulatory development strategy. Early-phase clinical studies serve a critical role in determining whether novel therapeutic concepts can be safely and effectively advanced toward larger later-stage clinical trials and eventual commercialization. Establishing this regulatory and clinical foundation is particularly important for innovative cellular immunotherapy approaches aimed at addressing difficult diseases such as acute myeloid leukemia (AML).

Based on the regulatory progress achieved to date and the development framework supporting this program, the TLV study represents a well-positioned effort to evaluate a novel therapeutic strategy in early clinical testing. Please find a Regulatory Strategy Timeline on the next page which includes the following anticipated FDA engagement milestones:

- **mid-Phase 1:** focused FDA interaction on emerging safety/biologic activity, potency strategy, assay development, and key CMC issues
- **end-of-Phase 1:** formal discussion of Phase 2 design, dose/regimen, endpoints, and the maturity of potency/product characterization
- **during Phase 2:** one interaction can be used to align on manufacturing evolution/comparability and another, if needed, on registrational study design or critical development issues
- **end-of-Phase 3 / pre-BLA:** formal pre-BLA interaction focused on content/readiness of the application, datasets, CMC, inspections, and submission logistics.

I appreciate the Committee's consideration of this proposal and its potential to contribute to the development of new treatment approaches for patients with AML.

Most sincerely,

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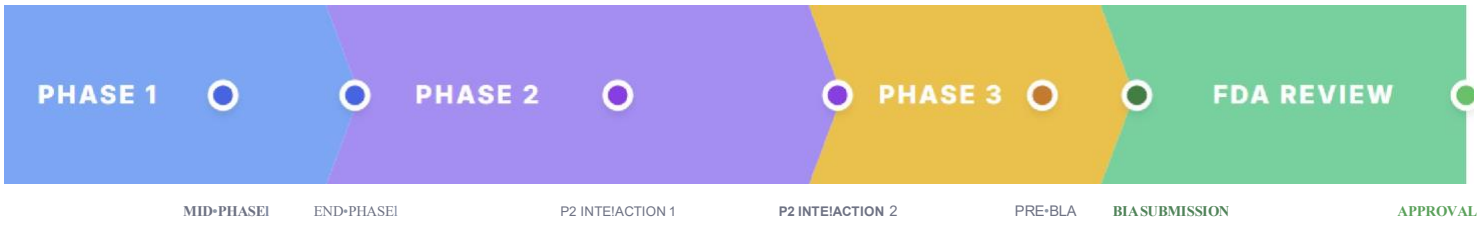
Biologics License Application (BLA) Pathway

FAST TRACK ORPHAN DRUG PRIORITY REVIEW

BLA Approval Target
8 Months Post-Submission

qRegulatory Strategy Timeline



01 Early Engagements

- **Mid Phase 1 FDA Interaction:** Focus on emerging safety, biologic activity, and assay development (CMC).
- **End of Phase 1 FDA Interaction:** Formalize Phase 2 design, dose/regimen selection, and potency maturity.

02 Phase 2 Clinical Development

- **Phase 2 FDA Interaction 1:** Manufacturing evolution and comparability (critical for biologics).
- **Phase 2 FDA Interaction 2:** Registrational study design or critical development issues.

03 Pre-BLA & Submission Prep

Phase 3 FDA Interaction: Content readiness, inspection logistics, and dataset formatting.

T·MINUS 4 MONTHS
Request Meeting

T·MINUS 2 MONTHS
Hold Interaction

04 Priority Review Execution

Filing Period — 60 Days

Review Period — • 11&

Office of Therapeutic Products (OTP) Guidance

The Pre-BLA meeting is a critical milestone for verifying the adequacy of clinical and CMC data packages. Per guidance from CBER OTP, we will ensure the meeting occurs no later than 2 months before submission to allow for dataset and CMC logistical alignment.