



USC University of
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RE: Letter for the January 29th CIRM Board Meeting

Dear CIRM Board,

We are grateful for CIRM's sustained support of our preclinical and clinical programs over the past seven years, which has been instrumental in advancing impactful translational research. Our laboratory has been competitive with two successfully completed CIRM projects through DISC2 and CLIN2 awards.

CIRM funding through the DISC2 award enabled the development of our ovarian cancer program, culminating in a clinical-stage CAR T cell therapy targeting tumor-associated glycoprotein 72 (TAG72). TAG72 is broadly expressed across ovarian, colorectal, gastric, and pancreatic cancers. This work directly led to a highly competitive NCI R01 award and the initiation of an ongoing Phase 1 clinical trial, which is already demonstrating safety and promising patient responses in women with recurrent epithelial ovarian cancer (rEOC).

That same DISC2 award also supported the development of a novel cytokine-engineering strategy that significantly enhanced T cell persistence and function. These advances resulted in several high-impact publications and the nomination of our next-generation clinical candidate. Our engineered fusion protein (anti-PD-L1-IL-12) that we secrete from CAR T cells simultaneously blocks a major immune checkpoint pathway that inhibits T cell activity in tumors and delivers a potent pro-inflammatory cytokine that rewires the tumor to be more responsive to CAR T cell therapy and to the body's own immune attack. This strategy builds directly on insights from our ongoing Phase 1 trial, and we are uniquely positioned to advance a Phase 1b/2 study of this novel TAG72-CAR/anti-PD-L1-IL-12 T cell therapy. This represents a non-incremental leap forward for solid tumor immunotherapy, with the potential to safely and robustly reprogram T cells for cancers that have historically been intractable. Beyond ovarian cancer, this platform establishes a blueprint for next-generation immune effector cell engineering across oncology, infectious diseases, and regenerative medicine. Despite its strong scientific and clinical rationale, this program has now been submitted twice for PDEV funding and failed to reach the preference threshold for a full application. Our latest PDEV submission utilized a non-viral gene delivery system, with a therapeutic that progressed from the previous DISC2 that targets an under-represented disease area with a novel approach that is distinct from CIRM's active awards portfolio.

Each year, more than 2,000 women in California are diagnosed with ovarian cancer. Over 60% present with peritoneal involvement at diagnosis, a hallmark of poor prognosis, and the five-year survival rate remains approximately 30%. There are no curative therapies for recurrent ovarian cancer. This is precisely the population our work is designed to serve, with the explicit goal of

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changing clinical practice and outcomes for these women. Cancer remains one of the most significant public health challenges in California, the United States, and globally.

While we recognize the promise of emerging iPSC, off-the-shelf, and *in vivo* cell engineering approaches, these technologies remain at earlier stages of development. In contrast, fundamental questions around target selection and engineering strategies for CAR T cells in solid tumors are best addressed using validated autologous platforms in the context of IND-enabling and early clinical trials. Importantly, progress using autologous systems with viral engineering creates a strong foundation for future alignment with companies developing allogeneic and *in vivo* approaches. CIRM is uniquely positioned to catalyze these partnerships, but only if it continues to support cancer-focused translational and early clinical programs.

The most recent PDEV and CLIN2 award cycles reflect a concerning exclusion of cancer-related programs and a pronounced bias toward industry-aligned allogeneic and *in vivo* approaches, which are admittedly at early stages of development with unknown impact for many diseases including solid tumors. This omission, driven largely by non-scientific preferences at the early stages of review, fails to address one of the most urgent unmet medical needs facing Californians. By the apparent de-prioritization of cancer, particularly high-mortality diseases including ovarian cancer, CIRM risks moving away from its core mission of advancing transformative therapies for patients with few or no treatment options. Californians living with cancer cannot afford for this need to be sidelined.

Sincerely,

A handwritten signature in black ink, appearing to read "Saul Priceman", written over a horizontal line.

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