CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Memorandum

To: Members of the ICOC
From: Jonathan Thomas
Re: CIRM Grant Review Process
Date: September 25, 2025

We recently received a letter from five California institutions regarding the outcome of the way CIRM implemented preferences in selecting which applications will receive a full grants working group review. That letter is attached here.

The goal of the Strategic Allocation Framework (SAF) is to ensure that CIRM's limited funds are translated into therapies, and to that end the SAF includes measurable goals that we believe are essential for driving new disease cures. We also included preferences in our program announcements that are intended to select for applications that are most likely to help us reach those goals.

I understand that the revised process is new to people, and the outcomes were therefor surprising. At the upcoming board meeting I will be reviewing the progress of the SAF, providing a budget forecast, and discussing how preferences move us toward our goals, and ultimately toward cures. At the January board meeting, we will be presenting a portfolio review that illustrates the effects of preferences over several application cycles.

I welcome the opportunity to enhance clarity around program priorities and ensure transparency about our processes. I and the entire CIRM Team are committed to listen to stakeholders and improve processes whenever possible.

September 15, 2025

Dear Independent Citizens' Oversight Committee,

We thank you for your service to CIRM, which has been a critical source of funding support and scholarly partnership for many translational and clinical projects across California. We are a group of Californian researchers who have been actively engaged in the development of novel therapies for diseases that impact patients in California and beyond, and we are writing to express concern about recent developments in CIRM's process of triaging grant proposals without scientific review, particularly with grant proposals that are poised to enter clinical testing and with the potential to improve patient lives. As you well appreciate, these programs are unique and likely will not advance with similar speed or determination without CIRM. We urge the ICOC to examine this new process and implement modifications that would ensure efficient use of CIRM funding on the most high-impact science that can translate to patient benefit.

After a pause of several months, CIRM reopened submission portals for several grant mechanisms earlier this year. Among these were PDEV (replacing the previous TRAN1 and CLIN1 mechanisms), DISC4, and CLIN2. In the PDEV and DISC4 mechanisms, pre-applications were requested, and CIRM explicitly noted a list of "preferences" that would be used to select proposals for full application. In the CLIN2 track, full applications were requested, and the Program Announcement did not state that any priorities would be used to triage applications based on administrative rather than scientific considerations. Nevertheless, the outcome of the PDEV, DISC4 and CLIN2 cycles this summer made clear that CIRM is now administratively eliminating a large number of proposals based on considerations that are unrelated to scientific merit, and in some cases inconsistent with stated CIRM goals of maximizing clinical translation, supporting therapies developed with prior CIRM funding, and focusing on indications such as CNS diseases. We provide several examples below to illustrate these concerns.

1. Prior TRAN1-funded therapies with successful pre-IND meetings triaged without scientific review in PDEV

Dr. Cristina Puig Saus and Dr. Lili Yang each developed a chimeric antigen receptor (CAR)-T cell therapy for cancer, and each completed a successful pre-IND meeting with the FDA with support from CIRM TRAN1 funding (TRAN1-12258 and TRAN1-12250, respectively). Dr. Puig Saus's pre-IND meeting was attended by CIRM program officer Dr. Ross Okamura, who saw first-hand that the FDA reviewers were very satisfied with the discussion and expecting the full IND package in the near future. Dr. Yang's technology is a hematopoietic stem cell (HSC)-derived therapy, thus her application met multiple PDEV preferences (stem cell-derived therapy, prior CIRM funding, and completed pre-IND meeting). And yet, both pre-applications by Dr. Puig Saus and Dr. Yang were triaged, and the rejection letters made clear that the decision was not based on scientific merit and instead based on administrative considerations.

2. Prior DISC2-funded therapy with successful nonclinical package primed for clinical translation triaged without scientific review in PDEV

Dr. Saul Priceman developed a cytokine-enabled CAR-T cell therapy for solid tumors, specifically ovarian and pancreatic cancers, with initial support from a prior DISC2 award (DISC2-11107). Dr. Priceman's cellular immunotherapy builds on an exciting NCI R01-funded phase-1 trial evaluating the same parental CAR-T cell therapy for patients with recurrent ovarian cancer. This novel cytokine-enabled CAR-T cell product shows powerful curative responses in

preclinical models with a promising safety profile, and would be rapidly translated to clinical testing in the next 2 years. However, the pre-application by Dr. Priceman, which builds on prior CIRM support and would utilize CIRM-supported USC's Alpha Clinic and the USC/CHLA cGMP Manufacturing Facility, was triaged without review of scientific merit.

3. CNS-focused application with fundable score in prior TRAN1 cycle triaged without scientific review in PDEV

Dr. Yvonne Chen submitted a PDEV pre-application focusing on a CAR-T cell therapy for glioblastoma (i.e., a CNS disease). This application was a more developed version of a prior TRAN1 submission that had been recommended for funding by the CIRM Grant Working Group (GWG) after rigorous scientific review in November 2024. However, the project was not funded at that time as the TRAN1 mechanism did not have sufficient funding remaining. Upon submission as a PDEV pre-application in the June 2025 cycle, this proposal was administratively triaged, despite meeting the priority of CNS disease and clearly being of scientific merit and interest based on prior CIRM GWG review.

4. CLIN2 applications with approved INDs prepared with prior CIRM funding triaged without scientific review

Dr. Antoni Ribas and Dr. Sarah Larson each submitted a CLIN2 application that was similarly triaged without scientific review. In both cases, the proposals involved successful INDs that had been prepared with prior CIRM funding (CLIN1-12946 for Dr. Ribas, and TRAN1-11555 for Dr. Larson in collaboration with Dr. Yvonne Chen). CIRM's Program Announcement for CLIN2 did not indicate that any administrative preference would be used to triage applications. Consequently, investigative teams spent significant amounts of time preparing full applications only to have them eliminated without any consideration for their scientific merit. The rejection letters provided identical language stating that each of these proposals "received an objective qualification score of 2 and ranked in the third tier of the objective qualification pool." However, CIRM never detailed the "objective qualifications" that may have been informative in preparation of the CLIN2 applications.

5. Neurological disease-focused DISC4 application leveraging prior CIRM-supported clinical data triaged without scientific review.

Dr. Christine Brown submitted a DISC4 pre-submission that strongly aligned with the FY25-26 preference topic of neurological diseases, focusing on high-grade gliomas (HGG). The proposal sought to interrogate unique patient cohorts and correlative samples from multiple phase-1 CAR-T cell trials in HGG/glioblastoma, including those developed and executed with CIRM support through prior TRAN1 and CLIN2 awards. Despite alignment with all programmatic priorities, including neurological disease focus and a cross-disciplinary, multi-omics approach with a mechanistic disease and biomarker discovery focus, the pre-submission application was administratively triaged.

We fully understand that in the current funding climate, CIRM is receiving more applications than can be reviewed in full detail. However, the pattern with which CIRM is rejecting proposals without any apparent consideration for scientific merit is deeply concerning. Furthermore, CIRM's stated objective of maximizing the efficient use of California taxpayer dollars to facilitate clinical translation is clearly inconsistent with repeated administrative rejections of previously CIRM-funded projects. This translates to therapies that have been developed with millions of

CIRM dollars that will now sit in limbo not due to scientific challenge, but due to CIRM's changing and unclear administrative priorities.

We urge the ICOC to review CIRM's current grant review process, and incorporate greater focus on the scientific merit and therapeutic potential of the proposed applications. As researchers and as California residents, we believe significant changes need to be made to enable CIRM to accomplish its stated mission in support of California's scientific endeavors. We would be very willing to provide feedback and suggestions if they would be helpful to the ICOC, and we look forward to the ICOC's response to this request.

Sincerely,

City of Hope®

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