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February 19, 2024

Independent Citizens Oversight Committee (ICOC)
Application Review Subcommittee (ARS)
California Institute for Regenerative Medicine (CIRM)
601 gateway Blvd, Suite 400
South San Francisco, CA 94080
c/o Claudette Mandac, cmandac@cirm.ca.gov
and Scott Tocher, stocher@cirm.ca.gov

RE: Continuation of clinical trial funding of gene therapy for Artemis-Deficient Severe Combined Immunodeficiency (ART-SCID) – CLIN2-10830

Dear Independent Citizens Oversight Committee
and Application Review Subcommittee, CIRM:

As Professors of Pediatrics and recognized experts in primary immunodeficiencies, we request that you allow us to submit a second CLIN2 application, without co-funding, by March 29, 2024, or as soon as possible, to allow us to complete our current clinical trial of lentiviral gene therapy for Artemis-Deficient Severe Combined Immunodeficiency (ART-SCID) without interruption. Our initial CIRM-funded first-in-human phase I/II trial (CLIN2-10830) began in 2018 and has treated 14 infants with ART-SCID, achieving 100% survival with T and B cell immune reconstitution, an unprecedented success compared with standard allogeneic transplantation. We have received Regenerative Medicine Accelerated Treatment (RMAT), Rare Pediatric Disease (RPD), and Orphan Drug (OD) designations from the FDA. At a Type B meeting in October 2023, the FDA encouraged us to complete the current trial and the final steps for submission of a BLA.

Although ART-SCID is a very rare disease, a founder mutation in Navajo and Apache Native Americans causes 1/2000 births to be affected in these underserved populations. Because of the small market for our treatment, we have been unable to secure corporate co-funding.

We were heartened, therefore, by the CIRM decision of December 14, 2023, to remove the co-funding requirement for non-profit applications, and we designed a second CLIN2 study with the collaboration of UCSF leadership, who are committed to upgrading our GMP facility to meet BLA standards and to sustain our cell product manufacturing in this academic setting. However, for over two months no changes have been made to the CIRM online template to allow us to submit our application. And now we have learned from the Flow Control Memo published in the Agenda for your February 22 meeting of a plan to accept no CLIN2 applications until after the June 2024 Board meeting. The funds from our first CIRM CLIN2 grant will be depleted by July 2024. Thus the proposed delay places us in jeopardy of having to close the trial, indefinitely delaying access to this most promising treatment for ART-SCID patients, including the Native Americans, who are underserved and underrepresented.

RE: Continuation of clinical trial funding of gene therapy for Artemis-Deficient Severe Combined Immunodeficiency (ART-SCID) – CLIN2-10830

CIRM has encouraged and funded our pre-clinical and clinical work on this project since 2013. We have successfully met all milestones and are on track to achieve our goal of licensing our lentiviral treatment with the FDA. Although ART-SCID is rare, our treatment is life-saving for California infants with ART-SCID as well as infants from underserved and underrepresented Native American populations. We hope that the ICOC will take this into consideration and will without further delay open the application process for a second CLIN2 without a co-funding requirement.

Sincerely yours,

Morton J Cowan, M.D.
Professor Emeritus of Pediatrics

Jennifer Puck, M.D.
Professor of Pediatrics