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STEIN EYE INSTITUTE
UCLA DAVID GEFFEN SCHOOL OF MEDICINE
CORNEA DIVISION
100 Stein Plaza, UCLA
Los Angeles, CA 90095-7003

October 15, 2019

Chairman Jonathan Thomas
Independent Citizens Oversight Committee
California Institute for Regenerative Medicine
1999 Harrison Street, Suite 1650
Oakland, California 94612

RE: CLIN2-11650: Safety and Feasibility of Cultivated Limbal Stem Cells for the Treatment of Limbal Stem Cell Deficiency, PI: Sophie X. Deng, MD, PhD; Stein Eye Institute, University of California, Los Angeles

To the ICOC Chairman and the Application Review Subcommittee:

I am writing to ask your support for our CLIN2 application to treat the blinding eye disease limbal stem cell deficiency (LSCD). We are thrilled that our application received a Tier 1 score from the Grants Working Group as we are ready to start the Phase I Clinical Trial that will test the safety and efficacy of our autologous limbal stem cell transplantation using a novel cultivation method and *in vivo* imaging technique.

Our work represents the only active corneal program in the entire CIRM portfolio. Most importantly, the proposed clinical trial is critical for patients as without adequate limbal stem cells, maintenance of a clear cornea isn't possible, resulting in pain, light sensitivity and vision loss, all of which have a profound impact upon quality of life. Cornea transplant is not a viable treatment for LSCD and will fail in these patients.

THE CLINICAL TRIAL BUILDS ON PREVIOUS CIRM SUCCESS

Should you choose to fund our application, ***this clinical trial will be the culmination of an active partnership between CIRM and UCLA that began in 2011***. This CLIN2 award will support the next stage of development of the therapy, e.g., clinical trial.

Owing to the vision of the CIRM Governing Board, your support for the last 8 years via a Discovery Stage award, a Bridge award and a subsequent CLIN1 award allowed us to successfully accomplish the goals of each grant and develop a stem cell therapy that is ready for clinical readiness in patients with severe/total LSCD affected in one eye or both eyes.

- ***IND & IRB Ready***: We obtained FDA IND and IRB approvals and are ready to initiate the trial.
- ***1st Therapy***: Our therapy represents the first that has the potential to treat bilateral severe disease using autologous limbal stem cells.
- ***1st Established Standardized Criteria***: We established the first standardized criteria to measure the disease severity and treatment efficacy.
- ***1st Global Consensus***: Our work on limbal stem cell deficiency laid a foundation of the first global consensus on the definition, diagnosis, classification and staging of LSCD.
- ***Milestone Track Record***: Our team has a track record of reaching every milestone on or ahead of the proposed timelines except in three occasions in which the progress was delayed due to factors that we had no control of such as availability of equipment and the government shutdown

that delayed the IND approval. With our track record, we are confident that we will have preliminary data on the safety and efficacy available before November 2020 if we have the support to start the trial in November, 2019.

- ***Publications***: Our work resulted in 37 peer-reviewed publications on limbal stem cells and LSCD
- ***Patents***: We filed two patent applications.

READY FOR THE CLINIC: ACCOMPLISHING THE CIRM MISSION

In keeping with CIRM's urgent mission, over the past three months to advance therapies quickly to the clinic, we have continued to prepare for the anticipated clinical trial. We completed the manufacturing of the necessary clinical grade raw materials, obtained IRB approval and identified several patients who are willing to participate in the study. As noted above, FDA approved our IND and once funded, we are ready for a seamless transition to the clinical trial.

We have the team, the expertise in clinical trials and manufacturing, the patient population, and the environment necessary to carry out the clinical trial. Many of my patients are eager to be enrolled, but we can't start and complete this clinical trial without partnering with CIRM. Furthermore, we have the support of the CIRM funded UCLA-UCI Alpha Stem Cell Clinic, a first-of-its-kind, cross-institutional "*Center of Excellence*" to overcome roadblocks and conduct stem cell clinical trials.

MEDICAL NEED: COMMITMENT TO PATIENTS

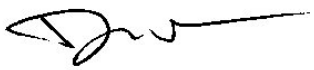
We are committed to improving outcomes for patients with LSCD. As a cornea specialist who cares for patients with LSCD and has seen their struggles, the impact of LSCD on patient's lives is immense. While we were developing our therapy, one of my patients passed away waiting for the treatment. During his final years, he lost interest in his life from the constant eye pain and poor vision resulting from LSCD, which deprived him of the ability to read, an activity that he most enjoyed. Another of my LSCD patients was so distressed after he became blind in one eye that he committed suicide. This is how much sight impacts life and this is what drives me to bring the best LSCD therapy to patients in the US.

Transplantation of autologous limbal stem cells has been demonstrated to have a far better long-term success (76% on average) and a much lower rate of eye complications than treatments using allogeneic source of limbal stem cells (average 42% success rate). In addition, long-term systemic immunosuppression is required for allogeneic limbal stem cell treatment but not for autologous treatment, and poses life threatening side-effects to patients. To date, the most effective and safe autologous treatment approach, which is by cultivation of patient's own stem cells is not available in the United States. The therapy is only feasible for patients affected in one eye. No effective autologous treatment is available for LSCD patients affected in both eyes. There is a clear need for a safer, more effective therapy for both unilateral and bilateral LSCD in the US and worldwide.

While we have secured a small amount of funding from the National Eye Institute (NEI), it is far from sufficient even to initiate the trial due to the limited amount that is dispensed each year. Nevertheless, the NEI support validates the importance of our work and the need for a safe and effective therapy for LSCD in the US. It is unlikely that the clinical trial will be funded by other sources. As laid out in proposition 71, the limbal stem cell project is appropriate for CIRM funding and aligns with the mission of CIRM.

On behalf of my patients, thank you for your consideration of this clinical trial.

Sincerely,



Sophie Deng, MD, PhD
Professor

MAILING ADDRESS: Jules Stein Eye Institute, 100 Stein Plaza, UCLA, Los Angeles, California 90095-7003, U.S.A.