CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

M E M O R A N D U M

TO: Members Of The Independent Citizens Oversight Committee

FROM: Ellen G. Feigal, M.D., Senior Vice President, Research and Development,
Ingrid Caras, PhD., Senior Science Officer

SUBJECT: Consideration of Extraordinary Supplement Award to DR1-01444

DATE: March 4, 2013

Background

On October 25, 2012, CIRM's governing board, the Independent Citizens Oversight Committee ("ICOC"), approved the concept proposal for Extraordinary Supplements to Existing Awards. The concept provided for "Level 1: Minor Supplements" as well as "Level 2: Major Supplements." The Level 2: Major Supplements are intended to "support grantees [in order] to enhance the probability of conversion of funded projects to unexpected and transformational benefits, and raise projects to a high probability of clinical benefit." This award provides for up to $3 million. CIRM is proposing that a Level 2 Major Supplement award in the amount of $3 million be provided to the Humayun Disease Team, DR1-01444.

In 2010, Mark Humayun and his team received a Disease Team I award in the amount of $15.9 million to develop a cellular therapy for dry Age Related Macular Degeneration (AMD) using retinal pigment epithelium (RPE) derived from human embryonic stem cells (hESC). An important component of this approach is implantation into the diseased area of the retina, of hESC-derived RPE grown in the form of a polarized monolayer on a synthetic substrate that mimics the natural Bruch's membrane in the eye, which is important for the attachment, survival and differentiation of RPE.

Progress on this project was evaluated by CIRM's Clinical Development Advisory Panel (CDAP) in July, 2011 and in July, 2012. Panel members were

extremely impressed by the team, the quality of the data presented, and the outstanding progress made and they strongly endorsed both the team and the approach.

The team is now entering the final stage of its Disease Team I project and is on track to file an Investigational New Drug (IND) Application by the end of the 4-year project period following completion of a series of Food and Drug Administration (FDA)-mandated, pivotal IND-enabling preclinical studies. Because the approach is extremely novel and pioneering, the precise regulatory requirements were not predictable at the outset. Consequently, it has become apparent that the original budget, which determined the amount of the award, is insufficient to cover all of the activities requested by the FDA to support the IND, and the team will therefore need supplemental funding to enable them to continue their strong progress towards filing an IND in order to be able to enter first-in-human clinical trials. The team has submitted to CIRM a formal request for Supplement funding to enable the completion of preclinical studies requested by the FDA.

Project Status and Proposed Use of Supplement Funds

In 2012, the Humayun Disease Team held a pre-IND meeting with the FDA prior to conducting critical activities for filing an approvable IND. In this meeting and subsequent follow-up discussions, the FDA had a number of specific recommendations regarding the preclinical studies to be conducted to support an IND filing, resulting in a more extensive and more expensive preclinical program than what had originally been budgeted for.

In January 2013, the team submitted to CIRM a formal request for supplement funding to enable them to complete the preclinical studies requested by the FDA. The submitted request included copies of FDA correspondence regarding the IND-enabling preclinical plan as well as a detailed budget and budget justification. The request was reviewed by the CDAP in February 2013.

The CDAP concluded that there is a clear preclinical plan that has been vetted by the FDA and a clear path forward to an IND; the budget and costs provided are reasonable and the team has the expertise to carry out the preclinical plan. The CDAP therefore recommended providing supplemental funding in order to ensure that the project stays on the critical path to filing an IND by the end of the 4-year project period.

Recommendation

Following endorsement by the CDAP, CIRM recommends that a Level 2 Major Supplement in the amount of $3M be awarded to the Humayun Disease Team so that it may conduct and complete the pivotal preclinical studies required to file an approvable IND, as recommended by the FDA in a recent pre-IND meeting and follow-up discussions with the Agency.