CALIFORNIA'S STEM CELL AGENCY

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

M E M O R A N D U M

July 15, 2014
From: Patricia Olson, Executive Director, Scientific Activities
To: Independent Citizens Oversight Committee (ICOC)
Subject: ICOC Agenda Item #11**:** Review Summary BF1-01768 submitted under the bridging supplement program

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The purpose of the CIRM Bridging Supplement Awards program is to accelerate development of stem cell therapies by providing a funding mechanism for the efficient and seamless advancement of promising CIRM-funded translational and development projects towards and through clinical development by "bridging" to further funding. CIRM approved submission of a full application, BF1-01768, for a supplement to a project funded under Early Translation II Awards (RFA 10-01). The application was reviewed and scored by external experts. The Application Review Subcommittee of the Independent Citizens Oversight Committee (ICOC) will make the funding decision based on peer review recommendation, any staff recommendation and a programmatic review by the ICOC. The review summary for this application accompanies this cover memo.

BF1-01768, Tier 1 (Score: 80)
Total Bridging Funding requested: $699,983

EXECUTIVE SUMMARY

This application is requesting additional funding to complete within 9 months the selection of a Development Candidate previously supported under a CIRM Early Translational Research Award. The goal of the original award was to develop a xenobiotic -free and feeder free culture system for the expansion of human limbal stem/progenitor cells for autologous transplantation to treat Limbal Stem Cell Deficiency (LSCD), a blinding eye disorder caused by cornea injury. While a similar product has been developed in Europe, this treatment is not available in USA. The team has tested multiple conditions and developed a method for ex-vivo expansion of limbal stem cells in a xenobiotic - free system on a culture substrate and scaffold derived from amniotic membrane. The expanded cells, together with the scaffold, will be transplanted into the diseased or injured eye to regenerate the injured cornea. There are two specific aims: 1) to optimize the amniotic membrane culture substrate; and, 2) to optimize the culture medium especially the human serum component.

Objective, Significance and Impact:

- The use of autologous expanded limbal stem cells transplantation to treat Limbal Stem Cell Deficiency (LSCD) is scientifically reasonable and has been already validated in clinical trials in Europe and Asia but the treatment is not available in US.

- There is an unmet medical need in the US, for the treatment of non-healing corneal epithelial defects resulting from LSCD.

- Autologous LSC expansion under xenobiotic free and feeder free conditions provides a route to approval for in the US for this candidate therapeutic.

- The TPP, while scientifically and clinically sound, lacks clarity as to the actual product to be developed.

- Reviewers would like to see further thinking on how the proposed product candidate would be developed and commercialized.

Responsiveness:

- This application is highly responsive since it proposes to further optimize a much-needed safe and acceptable treatment for limbal stem cell deficiency in the US.

- This proposal is focused on 2 specific aims to optimize and standardize the reagents and expansion procedures, both of which are logical and relevant extensions of the parent proposal now required

- The investigator has identified a next step for funding but has not developed a clear strategy with alternatives to enable further funding to move this project into preclinical clinical development.

Feasibility and Design:

- The PI has met milestones and made significant progress on the goal of establishing xenobiotic free and feeder free expansion conditions for LSC and developing and testing in a relevant in-vitro and in-vivo models.

- The proposed research is focused and logical and builds upon the prior work.

- Reviewers noted that there are inherent limitations in standardizing or further defining active components biologic reagents. Based on previous efforts in the field they considered weak proposed studies to further define active serum components. They encouraged a focus on the proposed studies that would define criteria for “acceptance” of reagents that would give an “active” therapeutic candidate.

- The proposed milestones are feasible and the proposed success criteria for each milestone provide quantifiable, meaningful measure(s) of outcomes and help advance the work in the proposed time period.

-The budget is reasonable for the activities proposed.

Assets, Collaborations, Resources and Environment

- The PI is a leader in this field and has a record of accomplishment.

- The PI has an excellent and appropriate team and has established critical scientific collaborations to successfully carry out the proposed project.

- Reviewers, while noting the likelihood of limited interest from large pharmaceutical companies, encouraged the PI to pursue strategic partnering/collaborations with organizations that could facilitate product development, licensure and treatment availability for patients.

- A patent application has been filed on the culture method but reviewers noted that work on other LSC expansion approaches in Europe and Asia has been done.

- All necessary resources are available and the environment is excellent.