CALIFORNIA'S STEM CELL AGENCY

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

M E M O R A N D U M

November 22, 2013

From: Alan Trounson, PhD., President; Bettina Steffen, MD., Associate Director, Development Activities; Ellen G. Feigal, MD., SVP Research and Development, and the Development and Early Translational Teams

To: Application Review Subcommittee, Independent Citizens Oversight Committee (ICOC)

Subject: Staff Recommendation for Tier 2 applications submitted under RFA 13-01, Duane Roth Disease Team Therapy Development (Disease Team 3) Awards

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In accordance with Section 7, Article V of the Bylaws of the Scientific and Medical Research Working Group and Section 6, Article VI of the Board's bylaws, both as amended on 3/19/13; the President and the scientific staff, following internal review and consideration would like the Application Review Subcommittee to consider the following.

Application #: DR3 -07281
Type application: Disease Team Award, preclinical, IND-enabling and early clinical trial
Tier, Average Score: Tier 2, 70
Title: Tissue Engineered Recellularized Laryngotracheal Implants
Disease Target: Tracheal transplant
Approach: Autologous stem / progenitor cells on a biologic scaffold
Requested funding: $13,277,369

Points for Consideration:

- This project focuses on developing tissue-engineered replacements for large airway disease, a potentially transformative area of regenerative medicine
- This project brings to California a novel technique and leverages more advanced work taking place in the UK
- The project would create the opportunity to model technology transfer in a complex engineered product, and to reproduce key preclinical data in an independent setting in a second, clinically relevant model
- The potential therapeutic would be tested and developed within California; and if the project advances into clinical development, early access would be available to citizens of California

- CIRM has no other hollow tube conduit tissue engineering approaches in the development portfolio. Such constructs are considered the logical entry point for 3-D replacement tissues

Staff Recommendation: Fund with condition. Approve limited funds (not to exceed $3M direct projects costs / up to $4.44 M total costs) up to 2 years for preclinical activities, including demonstration of manufacturing capability, comparability of the analogous product, and in vivo safety studies. This can include IND-enabling studies but will not include any clinical activities or GMP manufacturing for clinical use.

Application #: DR3 -07061
Type application: Disease Team Award, IND-enabling and early clinical trial
Tier, Average Score: Tier 2, 69
Title: Subretinal delivery of human neural progenitor cells for the treatment of retinitis pigmentosa
Disease Target: Retinitis Pigmentosa
Approach: Allogeneic human neural progenitor cells
Requested funding: $15,992,447

Points for Consideration:

- CIRM is funding two other Disease Teams and one Early Translational project aimed at retinal rescue or restoration. Different cell sources and target replacement cells are employed by the projects:
    - One Disease Team (DR2A-05739) is developing a cellular therapy for the same indication, Retinitis Pigmentosa
    - Another Disease Team (DR1-01444) uses a functionally polarized hESC-derived monolayer in Age-Related Macular Degeneration. A follow on project to conduct an early clinical trial is being presented today (DR3-07438) as Tier 1, Recommended for Funding
    - An Early Translational Award (TR4-06648) to develop hESC-derived "sheets" of retinal progenitor cells and retinal pigmented epithelial cells has recently been awarded

Staff Recommendation: Do not fund

Application #: DR3 -06945
Type application: Disease Team Award, early clinical trial
Tier, Average Score: Tier 2, 69
Title: Clinical Trial of Stem Cell Gene Therapy for Sickle Cell Disease
Disease Target: Sickle Cell Disease
Approach: Autologous HSC, genetically corrected ex vivo by lentiviral vector mediated addition of a hemoglobin gene that blocks sickling

Requested funding: $13,935,441

Points for Consideration:

- The project leverages the team and know-how gained in a Disease Team I project
- This project is at the most advanced development stage of the projects in the CIRM portfolio targeting blood diseases
- Sickle cell disease has a high unmet medical need and this approach allows for a chance to detect evidence of biologic activity early in the trial in support of CIRM's strategic goal to demonstrate clinical proof-of-concept

Staff Recommendation: Fund

Application #: DR3 -07078

Type application: Disease Team Award, Early Translation Allowance Pathway (IND-enabling studies and file IND)

Tier, Average Score: Tier 2, 67

Title: Embryonic Stem Cell-Derived Chondroprogenitor Cells to Repair Osteochondral Defects

Disease Target: Osteochondral defects

Approach: Allogeneic hESC-derived chondrocyte progenitors with a biologic scaffold

Requested funding: $13,423,503

Points for Consideration:

- The project leverages the team and know-how gained in a completed Early Translation project
- This project is at the most advanced development stage of Early Translation projects in the CIRM portfolio targeting cartilage disorders and uniquely focuses on a pluripotent-derived progenitor cell
    - An Early Translational Development Candidate Feasibility Award (TR3-05709) to develop an autologous dermis isolated stem cell-derived tissue engineered product for the treatment of focal cartilage defects recently initiated.
    - An Early Translational Award (TR2-01829) is a small molecule to induce chondrocyte differentiation of resident MSCs for the treatment of osteoarthritis.
- There are no funded Disease Team Awards or Strategic Partnership Awards in the CIRM portfolio in cartilage disorders

Staff Recommendation: Fund