CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Concept Proposal for an External Innovation Initiative

Moving innovative technologies into the clinic involves years of development, intensive resource investment, and navigating an evolving regulatory landscape. The California Institute for Regenerative Medicine (CIRM) is charged with advancing the development of potential cures and therapies based on stem cell science. To meet that Mission, an external review panel recommended in late 2010 adoption of "… a more aggressively proactive approach to identifying innovative projects across the stem cell therapeutic landscape that shows promise for moving into translational research, clinical trials and product development." Accordingly, CIRM here proposes an initiative to support new collaborations or "bolt on" (i.e., attaching a new collaboration to an existing, ongoing project) collaborative funding of research projects of CIRM-supported California investigators with teams that are making extraordinary progress outside California.

CIRM has established a collaborative network comprised of funding entities in 12 countries, 2 international states, 1 domestic state, and 2 foundations. Just recently, the National Institutes of Health (NIH) entered a collaborative relationship with CIRM. Through this collaborative external network, California investigators currently collaborate with their peers from outside the State on 19 projects. These collaborative projects range from tackling immune response issues such as probing the challenges in inducing immune tolerance to conducting collaborative IND enabling studies in a range of conditions that includes: Parkinson's Disease, HIV/AIDS, eye diseases, childhood neurological disorders and genetic diseases and cancer towards first in human studies. Through this network and other resources, CIRM can identify high quality, high impact work being done by stem cell researchers around the world. CIRM proposes to expand its ability to foster collaborations involving CIRM funded researchers and their out of state peers, wherever the innovative opportunity and expertise exists to potentially accelerate research leading to clinical proof of concept, through this new External Innovation Initiative.

The proposed structure of the External Innovation Initiative is a Program announcement with rolling submission applications, review by the GWG up to two times per year if an applicable review is not otherwise timely scheduled, with recommendations to the ICOC for final decisions.

Objectives:

- Accelerate development of stem cell therapies, (as set forth in Proposition 71)

- Supplement CIRM's existing RFA cycles with a mechanism that allows CIRM to more proactively and more quickly support engagement of California stem cell scientists in cutting edge, high impact research projects with their most advanced colleagues around the globe.
- Implement recommendation of the External Review Panel to *"*Pave a path from fundamental to translational research, translational medicine, product development and healthcare delivery" by a "Transition to a much more proactive strategy of funding that aligns CIRM's peer review and other processes with its mandate of delivering new treatments to the clinic as articulated in CIRM's mission and strategic goals*".*
- Implement the recommendation of the External Review Panel to adopt a "porous opportunity model rather than an internal pipeline model… [to] keep California as the hub of clinical proof of concept in regenerative medicine for the world rather than just for CIRM funded pipeline projects." (Recommendation 5)

Description of Program

- **The External Innovation Funding Program** would catalyze the collaboration between California researchers and researchers external to California through new collaborations or a "bolt on" program for funding of key staff as individuals or teams to substantially enhance an innovative aspect of a project or technology that would accelerate that study towards clinical applications particularly for projects which 1) warrant particularly speedy funding that cannot be addressed quickly enough through CIRM's regular RFAs; 2) have significant potential for high impact on the field, and 3) are already funded by another funder or are programs which will receive funding from another non-profit or government entity outside of California, but which could benefit from particular expertise resident in California, and could be jointly funded as part of a CIRM co-funding arrangement.

  The intent is to bring innovative, cutting-edge stem cell research and expertise from outside of California to work with CIRM-funded investigators offering complementary expertise and/or a unique scientific clinical environment, as well as to foster California research projects that can "bolt on" to particularly innovative or unique technologies or expertise outside of California. The program would provide up to 12 months of supplemental funding to: 1) an existing, already ICOC approved CIRM-funded research award to support the high impact external research opportunity; or 2) for a new project in California that is tied to an already funded or to be funded external research opportunity by another non-profit or government entity outside of California. Additional time could be considered for longer term opportunities. The external research opportunities would have been identified by collaborative funding partners or through an inventory of the research landscape e.g., conferences, publications or networking. A previously ICOC approved CIRM-funded researcher would be added as a collaborative partner to these projects through a supplement mechanism to the California award, or a new award could be made to the California researcher for a new project.

  - Projects proposed for supplemental funding under this program could include:

- Early and applied research on cutting edge technologies uniquely available outside of California that could be tied to the California component of the research
- Transfer of unique methods/ techniques from an investigator external to California that a CIRM grantee needs to move their translational program forward
- Preclinical/clinical development stage programs that require or could uniquely benefit from a California investigator and expertise external to California, providing the needed preliminary data to support the submission of a more comprehensive program in an emerging field critical to advancing stem cell science towards therapies

- Examples of potential projects:

The External California team would already be assembled and research external to California available for extension to California, or research already assembled within California could be "bolted on" to the unique opportunity outside of California. Foundations could participate, through a collaborative funding partnership, in the funding of any research component of the collaboration outside of California.

- The recent collaboration between CIRM and the National Institutes of Health (NIH) presents several potential opportunities for funding under this initiative due to the unique environment and resources available at NIH. For instance: the NIH Clinical Center and the Institutes and Centers that perform studies at the Clinical Center have access to cohorts of patients with rare and neglected diseases presenting the opportunity to conduct studies as well as to obtain tissue samples that may be used to generate iPSC lines; Potential opportunities for collaboration in translational projects particularly in the areas of Parkinson's Disease with derivation of cell lines, potential clinical studies, and HIV/AIDS linking NIH's CXCR4 programs with California's CCR5 world leading translation programs.

- Access to clinical investigator training or visiting fellowship programs; funding work in California that would benefit from access to special equipment or facilities at the NIH Clinical Center such as non-invasive imaging technologies for tracking cell fate, or access to the National Chemical Genomics Center to utilize their samples and assays in high throughput screening assays.

- An ongoing tools and technology, early translation or disease team project that may benefit from bolting on to innovative exploratory technology and expertise available at the Harvard Stem Cell Institute and one or more of its disease-focused programs in blood diseases, cancer, cardiovascular, diabetes, kidney, central nervous system or translational programs focused on early clinical studies.

- The application would need to include a plan for addressing intellectual property issues proactively. CIRM Intellectual Property regulations including access and pricing requirements would apply as set forth in CIRM's regulations, and both for-profit and non-profit entities are eligible to apply.

- CIRM proposes an External Innovations fund of $15 million, with maximum amount per 12 month period anticipated to be approx $500K. The fund is proposed to be subject to replenishment upon approval by the ICOC. Type of award, grant or loan, will be dependent on the amount and the organization requesting the funding.

    - Supplemental funding would provide a stipend for travel, partial salary support, accommodations (consistent with CIRM's Visiting Faculty awards) and research expenses of the external researcher working in California; if the investigator is from California with a California component of research, but must access unique expertise or resources directly at the external institute, funding would provide a stipend for salary and travel expenses, and laboratory support for critical elements, up to 12 months. Any other component of the collaborative research performed outside of California would be paid for by Collaborative Funding Partners or Foundations. Research anticipated to require more than a 12 month commitment would require the applicant, at the time of submission, to provide evidence of other potential funding sources satisfactory to CIRM, in its sole discretion, to complete the project after the 12 month funding from CIRM.

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