RFA 13-04: External Innovation Pilot Program

I. Purpose

The purpose of this RFA is to bring into California the most promising transformative research going on outside the state. CIRM is releasing this RFA as a pilot program. CIRM may modify the application procedures (through an amended RFA) if experience shows that a different process would be more effective and efficient.

II. Objective

The objective of this RFA is to catalyze the collaboration between California researchers and researchers external to California. This program would provide funding for key personnel in California to join innovative external studies in order to accelerate those studies towards clinical applications.

This RFA is intended to capture uniquely promising opportunities that cannot be addressed through CIRM's other funding programs. The program will be focused on new collaborations that:

- Involve California researchers in cutting edge technologies uniquely available outside of California
- Transfer unique external methods or techniques with the potential to advance the CIRM grantee's translational program
- Combine unique California and external expertise that will enable or accelerate development of preliminary data to support a comprehensive research program

III. Award Information

Under this Request for Applications (RFA), projects can range in duration from 12 months to 36 months, with justifiable direct project costs up to $500,000 per year. **This RFA is targeted at only the most exceptional proposals: CIRM expects to support only one or two such projects each year.** Given the urgency of CIRM's mission, all approved applications must be initiated (grant start date in issued and signed Notice of Grant Award) within 6 months of approval and authorization for funding by the Independent Citizen's Oversight Committee (ICOC), CIRM's

Governing Board, unless CIRM's President grants an extension based upon compelling justification of the need for additional time.

Progress on these awards is important to CIRM. Continued funding is contingent upon timely progress as outlined in the project plan and timeline established under the NGA.

CIRM and the agency funding the external research may decide to work together on the management/oversight of an approved collaborative, by participating in mutually agreed upon joint award administration activities. These activities may include but are not limited to participation in progress monitoring via progress reports.

IV. Award Mechanism

CIRM will fund approved proposals from non-profit and for-profit institutions (separately or in collaborations) through grants. Grant funds will be disbursed quarterly. Grant recipients are subject to all terms of CIRM's Intellectual Property and Revenue Sharing Requirements for Non-Profit and For-Profit Grantees (17 Cal. Code Regs. § 100600 et seq.).

Before funding contracts are signed, successful applicants must have a signed written agreement adequately addressing Intellectual Property (IP) issues relating to the collaboration with the external researchers, and must provide CIRM with copies. These IP Agreements will be reviewed by CIRM to ensure that they are consistent with CIRM's applicable IP regulations.

Research funding agencies or foundations could participate, through a collaborative funding partnership, in the funding of any research component of the collaboration outside of California.

V. Eligibility

A. Institutional Eligibility

Both non-profit and for-profit organizations are welcome to apply. At the time of the application deadline, the applicant organization must be conducting or managing research that is taking place in California. If these requirements are not met, CIRM may terminate all further action on the application.

"Non-profit organization" means: (1) a governmental entity of the state of California; or (2) a legal entity that is tax exempt under Internal Revenue Code section 501(c)(3) and California Revenue and Taxation Code section 23701d.

"For-profit organization" means: a sole-proprietorship, partnership, limited liability company, corporation, or other legal entity that is organized or operated for the profit or financial benefit of its shareholders or other owners.

CIRM encourages collaborative endeavors between non-profit and for-profit organizations.

B. Principal Investigator (PI) Eligibility

The PI must have an M.D., Ph.D. or equivalent degree, and must be authorized by the applicant institution to conduct the proposed research in California. By the application deadline, the PI must:

- Be an independent investigator in California at a non-profit applicant institution, or have an equivalent position and be an employee in California (at least 50-percent time) of a for-profit applicant institution
- Have documented authority from the applicant institution to staff the proposed project
- Have documented commitment from the applicant institution to provide laboratory space and shared resources sufficient to carry out the proposed research

Because of the need to move these projects forward quickly, the applicant PI must be a senior investigator with a recognized track record of successful progress on funded research projects, demonstrated as PI or Co-PI on a CIRM research award, or as the PI on multiple NIH research awards. No PI may submit more than one LOI per year under this RFA.

C. Co-Principal Investigator (Co-PI) Eligibility

This RFA does not allow designation of a Co-PI.

D. Project Eligibility

The application must propose a collaboration with an existing external research project. The external project must be led by a PI based outside of California, with funding in place for the duration of the proposed collaboration. (The CIRM award may extend for a short period beyond the end of the external funding, if justified by the need to complete work undertaken through collaboration.) The external (non-California) team must already be assembled and research external to California must be available for extension to California.

The scope of the proposed collaboration should be consistent with CIRM's scientific priorities:

> Projects investigating potential therapies are limited to therapies derived from human pluripotent stem/progenitor cells, or those that convincingly target endogenous stem cells in an innovative way.

Projects developing tools or technologies to advance stem cell research should be directly applicable to the use of human cells.

Basic research projects must utilize human stem cells, reprogrammed cells or their derivatives, and these cells must be necessary to achieve the outcomes of the proposed research.

E. Percent Effort Requirements

CIRM, mindful of the urgency of its mission, will only fund PIs who are willing to devote substantial, focused attention to the project. For this RFA, PIs must be willing and able to commit a minimum 20% effort.

F. Extraordinary Exceptions

The President of CIRM has the discretion to permit exceptions to any eligibility requirement specified in this Section V. The President may permit an exception if he determines, in his individual discretion, that the applicant has demonstrated that the exception would preserve an important research opportunity or make a critical contribution to one of CIRM's mission objectives. Exceptions must be consistent with the objectives of this RFA and the requirements of Proposition 71 as well as California state regulations, including the Grants Administration Policy (see Section XIII of this RFA) or they will not be considered.

If CIRM determines that an application does not meet the eligibility requirements, CIRM may terminate all further action on the application. To request an exception, or for assistance in determining whether one is necessary, contact the CIRM staff listed in Section XII.

VI. Relationship to Collaborative Funding Partner Program

Under CIRM's existing Collaborative Funding Partner (CFP) program, CIRM joins with other research funding agencies to fund research collaborations between California scientists and researchers in other states or countries. Most of CIRM's regular RFAs include the participation of CFP funders, and the CFP program will continue to be the primary avenue for CIRM support of collaborative research projects. Information about that program is available at: http://www.cirm.ca.gov/our-funding/stem-cell-research-collaborative-funding-agreements.

This External Innovation Pilot Program is aimed at potential projects that would not fit within the established CFP program. Examples would include:

- The non-California PI is not eligible for funding from one of CIRM's CFP partner agencies.
- The external project is already fully funded.

- The proposed new California project is a limited extension of the existing external project, and is not intended to achieve the types of goals required under CIRM's regular RFAs.

For collaborations proposed as part of this program, CIRM encourages CFPs and other funders to offer additional funding to the external project to facilitate collaboration with California researchers. Reviewers will consider additional external funding to be a positive factor in review.

VII. Notification Regarding Disclosure of Information

All applicants are hereby notified that CIRM may share Letters of Intent, full Applications and related information submitted by applicants with the agency or agencies funding the External Project. If the application is approved, CIRM may also share progress and outcome information with the external funder(s). All such disclosures will be subject to appropriate confidentiality agreements. If you have any questions about this policy, please contact Ian Sweedler (see Section XII).

VIII. Application and Evaluation Process

A. Letter of Intent

Prior to submitting an application, a PI must submit a Letter of Intent (LOI) describing the proposed project. CIRM will evaluate the LOI and decide whether to invite a Full Application for the proposed project. That decision will be made under the direction of CIRM's President.

Evaluation of an LOI will consider two primary criteria: Whether the external collaboration is critical to the proposal, and whether the proposed research is novel and transformative. The external collaboration would be considered critical if the project depends on unique expertise, methods, technologies or resources that are offered by the external collaborator, and unlikely to be available within California.

Assessment of the proposed research will be based on the type of work proposed:

- For a proposal that focuses on a therapeutic candidate, CIRM will consider whether the proposed therapeutic candidate would be likely to have a significant impact on standard-of-care management of the target disease/injury, and if it would offer advantages over current therapies on the market, or those that are in late stage development or the subject of research CIRM is already funding. CIRM will also consider the potential for the proposed research to advance the field of stem cell-based/regenerative medicine.

- For a proposal that focuses on stem cell biology, CIRM will consider whether a successful outcome would challenge dogma or resolve a critical bottleneck in the field of basic stem cell biology.

- For a proposal that focuses on tools and technologies for stem cell research, CIRM will consider whether the project would have a major impact on potential applications of stem cell research and regenerative medicine, rather than incrementally advancing the field.

The Applicant will be notified once CIRM has decided whether to invite a Full Application.

B. Full Application

If invited to submit a Full Application, an applicant will be notified of the review criteria that will apply. Because this program could encompass different types of projects, different review criteria may be appropriate. As with all of CIRM's RFAs, the general review criteria, described in Section IX, will be adapted to the type of project being considered, based on the goals and scope of the project. The specific review criteria will be based on recent CIRM RFAs for basic, translational or clinical stage research. CIRM will also provide application forms and instructions that are appropriate to the type of project proposed.

As described in the next section, Full Applications will be evaluated by CIRM's Grants Working Group (GWG). The GWG meets several times a year to review applications submitted under CIRM's regular RFAs, with reviewers selected for expertise relevant to that round of applications. If an applicant is invited to submit a Full Application, CIRM will provide an application schedule that will allow for review at an appropriate GWG meeting. The GWG will make funding recommendations to the ICOC, which will make final funding decisions.

CIRM's confidentiality and conflict screening rules will apply to everyone who will have access to applications or who will attend the review meeting, including CIRM staff, external reviewers, and representatives of Collaborative Funding Partner Agencies.

IX. Review Criteria

Stated below are the general review criteria for CIRM research award applications, modified to reflect the particular goals of this RFA. The specific criteria for a full application will depend on the nature of the proposal. As described in Section VIII, an applicant invited to submit a full application will be informed of the review criteria to be applied to that proposal.

Impact and Significance. Whether and to what extent the proposed collaborative research addresses an important problem; significantly moves the field forward, either scientifically or medically; moves the research closer to therapy; and changes the thinking or experimental or medical practice in the field.

Quality of the Research Plan. Whether and to what extent the proposed collaborative research is planned carefully to give a meaningful result; acknowledges the possible difficulties and provides for alternative plans should the proposed strategy fail; proposes a timetable that allows for achieving significant research or clinical results; and uses appropriate milestones to assess progress towards the aims and goals of the proposal.

Innovation. Whether and to what extent the proposed collaborative research approach is original, breaks new ground, and brings novel ideas, technologies or strategies to bear on an important problem.

Feasibility. Whether and to what extent the aims of the collaborative research can be reasonably achieved and the investigator has access to appropriate technology to perform the research.

Investigators. Whether and to what extent the California and external investigators have the training and experience to carry out the proposed project, including the investigators' record of achievement in the areas of pluripotent stem cell and progenitor cell biology, unless the research proposal is determined to be a vital research opportunity.

Collaboration. Whether and to what extent the proposal supports collaborative efforts that are essential to the aims of the work to be funded by CIRM, and that would allow the California investigators to make effective use of the unique expertise or resources offered by the external investigators.

Responsiveness to RFA. Whether and to what extent the proposed collaborative research project or activity adequately and appropriately addresses the goals and objectives of the RFA, as described in Section II.

Eligibility for Federal Funding. Whether and to what extent the proposed collaborative research is ineligible or unlikely to receive federal funding. If not, whether and to what extent the research is sufficiently compelling in that it presents "a vital research opportunity" that will materially aid the objectives of CIRM.

X. Application Procedure

A. Letter of Intent (LOI)

A PI may submit an LOI for this RFA using the forms and instructions provided in the Grants Management Portal at https://grants.cirm.ca.gov. To begin an LOI, send an email to ExternalInnovation@cirm.ca.gov, stating that you would like to create a Letter of Intent, and your Username on the Grants Management Portal.

The LOI should concisely describe the existing external project and the proposed California collaboration, and explain how they meet the criteria described in Section

VIII.A. above. The LOI must include a letter from the PI for the external project, endorsing the proposed collaboration and confirming information about the source and amount of financial support for the external project.

B. Full Application Forms

CIRM will only accept Full Applications that have been invited by CIRM, after review of an LOI. The PI and project must be those identified in the LOI; otherwise, the Application is deemed ineligible.

As explained in Section VIII, CIRM will provide the forms and instructions based on the LOI.

XI. Schedule of Deadlines and Reviews

Letters of Intent can be submitted at any time. In general, LOIs will be evaluated on a quarterly basis.

As explained in Section VIII, CIRM will provide an application and review schedule for each Full Application invited. The project described in the full application must be that described in the LOI. For most CIRM award programs, scientific review and final award decisions are completed 5 to 7 months after the date the full application is due.

XII. Contacts

For information about this RFA or the review process:

Ellen M. Feigal, M.D.
Senior Vice President for Research and Development
Email: efeigal@cirm.ca.gov
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XIII. CIRM Regulations

Grant awards made through this RFA will be subject to CIRM regulations. These regulations can be found on CIRM's website at http://www.cirm.ca.gov/reg/default.asp.

A. CIRM Grants Administration Policy

CIRM's Grants Administration Policy (GAP) for Academic and Non-Profit Institutions (Non-Profit GAP) and the GAP for For-Profit Institutions (For-Profit GAP) serve as the standard terms and conditions of grant awards issued by CIRM. All research conducted under this award must comply with the stated policy. Progress reports of research, as required by the GAP, are important to CIRM: Funding from year to year will depend on adequate scientific progress as outlined in the grant application timeline. CIRM's GAP is available at http://www.cirm.ca.gov/our-funding/our-regulations/stem-cell-regulations-governing-cirm-grants#GAP

B. Intellectual Property Regulations

CIRM has adopted intellectual property and revenue sharing regulations for non-profit and for-profit organizations. By accepting a CIRM Grant, the Grantee agrees to comply with all such applicable regulations.

C. Human Stem Cell Research Regulations

As reflected in CIRM's GAP, CIRM has adopted medical and ethical standards for human stem cell research (Title 17, California Code of Regulations, sections 100010-100110 available at http://www.cirm.ca.gov/our-funding/our-regulations/stem-cell-regulations-governing-cirm-grants#standards). All research conducted under this award will be expected to comply with these standards. This information can be found on the CIRM website.

D. California Supplier Regulation

CIRM has adopted a regulation to implement the requirement in Proposition 71 that grant and loan recipients make a good faith effort to achieve a goal of purchasing more than 50% of their goods and services from California suppliers (Title 17,California Code of Regulations, section 100502). Grant and loan recipients are required to comply with this standard.

E. Clinical Trial Registration

CIRM requires that any clinical trial funded under any of its funding programs be listed on http://clinicaltrials.gov/. CIRM will also require awardees to share the results, at the completion of their studies for the benefit of the field.