CIRM2.0
CALIFORNIA'S STEM CELL AGENCY

Partnering Opportunity for Discovery Stage Research Projects: The Quest Awards

DISC 2

PROGRAM ANNOUNCEMENT

12.28.16

Partnering Opportunity for Discovery Stage Research Projects:

The Quest Awards

DISC 2

Objective

The mission of California Institute for Regenerative Medicine (CIRM) is to accelerate stem cell treatments to patients with unmet medical needs.

The objective of the Discovery Program is to support exploratory research aimed at the discovery of novel stem cell technologies and related technologies to improve patient care.

This Quest Awards Program will promote the discovery of promising new stem cell-based technologies that could be translated to enable broad use and ultimately, improve patient care. Projects funded through the Quest Awards should propose technology that is uniquely enabled by human stem/progenitor cells or directly reprogrammed cells, or uniquely enabling for the advancement of stem cell-based therapies.

Project Outcome

The expected outcome at the conclusion of a Quest Award is identification of a novel candidate therapeutic, diagnostic, medical device, or tool that can immediately progress to translation activities to enable broad use (see section 'Award Information' for additional detail.)

To incentivize rapid progress to translation, Quest Award recipients who successfully complete a "Progression Event" within one year of the Quest Award end date will receive a Progression Award of $150,000 in direct project costs. CIRM defines a Progression Event as the successful acquisition of funding for subsequent translation of the Quest Award candidate either by the original award recipient, if appropriate, or by a qualified team to whom the original award recipient has "passed the baton". Quest Award recipients who demonstrate to CIRM successful achievement of a Progression Event within one year of their Quest Award conclusion will receive a Progression Award, which must be utilized for stem cell research relevant to CIRM's mission. Progression Awards will be administered using the mechanism described for Inception Awards (DISC 1).

Award Information

How much funding can CIRM provide and for how long?

CIRM will fund direct project costs of up to $700,000 per award to achieve a candidate that is a diagnostic, a medical device or a tool; or up to $1.4M per award to achieve a candidate that is a therapeutic. Direct project costs must be adequately justified and are subject to adjustment prior to the issuance of an award based on assessments by the Grants Working group (GWG), the CIRM team, or by the Application Review Subcommittee of CIRM's Governing Board. The proposed project period must not exceed 2 years.

What activities will CIRM support?

CIRM funds will support the following activities under this opportunity:

✓ Activities that will lead to selection of a novel candidate therapeutic, diagnostic, medical device, or tool ready for translation to enable broad use and ultimately, improve patient care including:

  ✓ Determination of medical need(s) and user needs to be addressed by the proposed candidate, and the technical requirements to meet these needs

  ✓ Develop and implement methods to identify/test/characterize candidate (or prototype) therapeutic, diagnostic, medical device or tool

  ✓ Technical feasibility and initial reproducibility assessment

  ✓ Characterization/testing of candidate(s) (research prototype(s), component research prototypes); determining mechanism of action, where applicable

  ✓ Scientific proof of concept studies relevant to intended use with candidate (research prototype)

  ✓ Develop a Target Product Profile (or Product Concept Document, see Appendix) for candidate therapeutic, diagnostic, medical device or tool

  ✓ Preparation for and conduct of stage appropriate regulatory meetings (e.g. for stem cell based cell therapeutic candidates - a pre-pre IND meeting)

CIRM resources cannot be used to support the following activities under this opportunity:

● Research lacking a strong rationale for the unique necessity of human stem/progenitor cells or directly reprogrammed cells to achieve the expected outcome OR research uniquely enabling for the advancement of stem cell-based therapies that does not include testing with human stem/progenitor cells or directly reprogrammed cells to achieve the expected outcome

● Generally, activities directly supported under CIRM's translation or clinical stage program announcements (see www.cirm.ca.gov)

CIRM 2.0

CALIFORNIA'S
STEM CELL
AGENCY

What is the expected outcome of a Quest Award?

The expected outcome of a Quest Award is a new candidate therapeutic, medical device, diagnostic or tool that is ready for translational stage activities. Criteria defining readiness for translation for each type of candidate include the following:

Therapeutic:

- A candidate therapeutic identified

- A draft Target Product Profile (see Appendix) developed

- Measures of identity, activity and purity developed

- Reproducible disease/injury modifying activity demonstrated with the candidate in preclinical model(s) relevant to the target indication(s)

- Initial studies performed assessing mechanism of action, pharmacokinetics (PK) (bio-distribution) and early safety

- For allogeneic stem cell based cell therapies:

    o Cells meet the Good Tissue Practices requirements for donor eligibility, or there is plan in place to address (donor eligibility requirements are described here.)

Diagnostic:

- A candidate diagnostic identified

- A draft Target Product Profile (or Product Concept Document, see Appendix) developed.

- Demonstration of technical feasibility: tests with diagnostic candidate (research prototype, component prototype) show that it will be feasible to meet product design requirements.

- Demonstration of scientific proof of concept

    o Testing with the diagnostic candidate (research prototype, including technology, biomarkers) demonstrates that analyte can be reproducibly measured at biologically relevant levels for the intended use in sufficient samples to distinguish relevant differences within the target population.

    o If the diagnostic is not stem cell based, then testing with human stem/progenitor or directly reprogrammed cells demonstrates its utility to address a critical bottleneck to the discovery, development or use of stem cell-based therapies.

Medical Device:

- A candidate medical device identified

- A draft Target Product Profile (or Product Concept Document, see Appendix) developed

- Demonstration of technical feasibility: Tests with device candidate (research prototype) show that it will be feasible to meet product design requirements.

- Demonstration of scientific proof of concept:

- o In test model(s) relevant to the intended use, the medical device candidate (research prototype) meets initial performance criteria

- o If the device technology is not stem cell based, then testing with human stem/progenitor or directly reprogrammed cells demonstrates its utility to address a critical bottleneck to the discovery, development or use of stem cell-based therapies.

Tool

- A candidate tool identified

- A draft Target Product Profile (or Product Concept Document, see Appendix) developed

- Demonstration of technical feasibility: Tests with tool candidate (research prototype) show that it will be feasible to meet product design requirements.

- Demonstration of scientific proof of concept:

  - o In test model(s) relevant to the intended use (must be a critical bottleneck to advancement of stem cell therapies), the tool candidate (research prototype) meets initial performance criteria

  - o If the tool/technology is not stem cell based, then testing with human stem/progenitor or directly reprogrammed cells demonstrates its utility to address a critical bottleneck to the discovery, development or use of stem cell-based therapies.

How will funds be awarded?

- Awards to successful applicants will be in the form of a grant.

- CIRM will disburse funds pursuant to a Notice of Grant Award.

Eligibility

What types of projects are eligible for partnering?

To be eligible, the proposed project must satisfy the following requirements:

(1) The applicant must propose studies for a new technology that is uniquely enabled by human stem cells or uniquely enabling for the advancement of human stem cell based therapies as follows:

- Discovery research for a novel therapeutic candidate

  - o that is stem cell based - where human stem, progenitor, or directly reprogrammed cells either compose the therapy or are used to manufacture the therapy

  - o that stimulates, recruits or targets endogenous stem cells or cancer stem cells

  - o where human stem, progenitor or directly reprogrammed cells are uniquely required for candidate identification and testing

- Discovery research for a novel human stem cell-based diagnostic, assay or tool candidate that can be used to discover, advance, monitor, or evaluate new therapies, OR

- Discovery research for a novel technology (a device, diagnostic or tool candidate) that proposes proof of concept testing with human stem, progenitor or directly reprogrammed cells and that addresses a critical bottleneck to the discovery, development or use of stem cell-based therapies

(2) The applicant must be ready to initiate work on the funded project within 120 days of approval.

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within 120 days of approval and authorization for funding by the Application Review Subcommittee of CIRM's governing board, the Independent Citizens' Oversight Committee ("ICOC").

(3) Co-funding is not required.

If the project requires funding over and above that which CIRM provides to achieve the expected outcome, documentation demonstrating the commitment of funds to cover the required additional amount must be provided by the application deadline (e.g., copy of executed term sheet showing amount of co-funding, conditions and source).

(4) For-profit organizations must demonstrate solvency.

For-profit organizations must provide documentation that shows 180 days cash on hand from date of application submission and the financial ability to meet the co-funding and contingency requirements for the term of the project. The determination of solvency will be made at CIRM's sole discretion.

(5) Application must be accurate and complete

All required components of the application must be completed and may not contain false or inaccurate information.

Who can apply and on what activities may funds be spent?

Only California Organizations are eligible to apply. A California Organization is a for-profit or non-profit organization that employs and pays more than 50% of its employees in California.

Allowable Project Costs include:

- Costs for activities conducted in California; and

- Costs for activities conducted outside of California, provided that the California Organization exercises direction and control over the activities.

Allowable Project Costs do **NOT** include the costs of activities performed by a separate out-of-state organization that retains intellectual property or publication rights in any intellectual property (e.g., invention, technology, data) arising out of the CIRM funded project.

CIRM may determine, in its sole discretion, whether an applicant is a California organization and whether the project activities are allowable.

CIRM 2.0

CALIFORNIA'S
STEM CELL
AGENCY

The applicant must demonstrate by the application deadline a commitment of funds from other sources for non-allowable project activities that are necessary to achieve the goals of the application.

Who can serve as the Principal Investigator (PI)?

To be eligible, the PI must satisfy the following requirements:

- Must be an employee of the applicant organization or be accountable for the conduct of the proposed project to the applicant organization through a formal contract.

- Must commit at least 20 percent effort to working on the project.

- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI.

Schedule and Deadlines

Applications Due*	February 15, 2017. For future application offerings, due date will be posted at www.cirm.ca.gov
Grants Working Group (GWG) Review	Approximately 90 days post submission
ICOC Review and Approval	Approximately 150 days post submission
Award Start	Must start within 120 days of award approval

* It is anticipated that applications under this program announcement will be accepted at approximately six-month intervals. Further information on subsequent offerings can be found at www.cirm.ca.gov

Application Review Information

What is the process for evaluating an application?

Pre-submission Consultation

In accordance with CIRM's mission, the Agency is committed to helping develop promising stem cell-based technologies by partnering with world-class investigators. Therefore, prospective applicants are encouraged to contact CIRM before applying with questions or to discuss their project's eligibility.

Eligibility Review

CIRM will assess whether the proposed project meets eligibility requirements sought under this program. If CIRM determines, in its sole discretion, that an application does not meet the eligibility requirements of the program or that the submitted

application is incomplete or contains false or inaccurate information, CIRM will notify the applicant of its decision, allow an opportunity to remedy, and if not remedied in a timely manner satisfactory to CIRM, terminate all further action on the application.

Scientific Review

The scientific merit of each application will be assessed by the GWG, which is composed of fifteen subject matter experts from outside California, seven patient advocate members of the ICOC, and the Chair of the ICOC. The list of scientific members who may participate in the GWG review can be found on the CIRM website. The composition of the ICOC can be viewed on the CIRM website.

The fifteen participating scientists on the GWG will evaluate the applications and score them according to scientific and technical merit, applying the review criteria described below.

If the number of applications received in any given cycle is significantly in excess of the number that the GWG can review in a single session, GWG members will conduct the review in two stages. In the first stage, reviewers will conduct a pre-review of applications to advance a subset of applications to second stage, the full GWG review described below. Those applications that are not advanced to the second stage will not be recommended for funding.

The Application Review Subcommittee will make final funding decisions giving consideration to the GWG recommendations and any CIRM team recommendations.

Consideration of Past CIRM Award Information (If Applicable)

The GWG may consider information from a previously funded and related CIRM award as part of its review. CIRM will provide the GWG with objective information regarding a related award that CIRM, in its sole discretion, deems relevant, including but not limited to achievement of specific milestones, data, and outcomes for a related CIRM award or awards.

A "related CIRM award" includes: (1) an award for which the applicant PI served as the PI, a co-PI, a co-investigator, or otherwise substantially participated in the conduct of the award; (2) an award involving the same research project or product; or (3) an award that includes overlapping team members.

Confidentiality

CIRM's confidentiality and conflict screening rules apply to everyone who will have access to applications or who will attend any review meeting in which confidential information is discussed, including but not limited to CIRM team members, reviewers and members of the ICOC. (Per Gov. Code §6254.5(e), non-public records may be disclosed to government agencies under confidentiality agreements.)

How will the scientific merit of an application be evaluated?

Scientific and patient advocate members of the GWG will evaluate applications and the scientific members will score them based on the following key questions:

1. Does the project hold the necessary significance and potential for impact?

Is the proposed technology likely to result in a candidate that could impact an unmet medical need? Would the expected candidate accelerate or increase the likelihood of successfully developing a stem cell technology that significantly improves patient care or that address a critical bottleneck to the discovery, development or use of

stem cell-based therapies? Has the applicant presented thoughtful options for progression from successful candidate discovery to translation?

2. Is the rationale sound?

Is the proposed project based on sound scientific rationale? Is the preliminary data compelling and supportive of the proposed project? Is the proposed project uniquely enabled by human stem/progenitor cells or directly reprogrammed cells, or uniquely enabling for the advancement of stem cell-based therapies?

3. Is the project well planned and designed?

Is the project appropriately planned and designed to meet the expected outcome of the program announcement to achieve a candidate ready to advance to translation? Is this a well constructed, quality project? Are potential pitfalls identified and alternative approaches presented? Do the project plan and timeline demonstrate an urgency that is commensurate with CIRM's mission?

4. Is the project feasible?

Are the proposed milestones and expected project outcome logical and likely to be achieved within the proposed timeline? Is the proposed team appropriately qualified and staffed? Does the team have access to all the necessary resources to conduct the proposed activities? Is the budget appropriate for the research proposed?

Application Components and Submission

How does one apply?

Applications must be completed and submitted online using the [CIRM Grants Management Portal](). Any prospective PI must create a login in the system to access application materials and apply. Applications are available in the system only to the PI. A PI may submit only a single Quest Award application in a given review cycle.

What components does an application include?

The Grants Management Portal provides instructions for completing all the necessary components and submitting a final application. The application is designed to collect information necessary to appropriately evaluate the proposal and for CIRM to rapidly initiate an award if approved for funding. Applicants are required to indicate key personnel involved in the project, describe how the proposal addresses the objective of the partnering opportunity, provide a detailed plan of proposed activities, and prepare and justify an appropriate budget.

The main components of the application include the following key sections:

1. **Application Preview Page:** This section will be utilized by reviewers to prescreen applications and select a subset to move forward to the second and final stage of review.

    o Project Summary
    o Area of Impact

o Vision for Progression

2. **Resubmission Statement:** If this application is a resubmission then the applicant will provide a brief statement on how this application addresses the reviewers' critiques.

3. **Statement of Significance and Impact:** Description of how the proposed candidate, if successful, could a) impact an unmet medical need, and/or b) accelerate or increase likelihood of successfully developing a stem cell technology that significantly improves patient care. If the candidate is not stem cell based, describe further how it could c) address a critical bottleneck to the discovery, development, or use of stem cell-based therapies.

4. **Objective and Milestones:** A concise description of the project objective and project milestones (template provided), and criteria for success.

5. **Rationale:** Description of the scientific rationale for the proposed research and the preliminary data.

6. **Research Plan**: A concise but detailed description of methods and techniques to be employed to achieve milestones, and potential pitfalls and alternative approaches.

7. **Timeline**: Activities-based timeline for achieving project milestones.

8. **Principal Investigator and Team:** A description of the PI and team's expertise and experience.

9. **Resources and Environment:** A brief description of the resources available to the project and environment.

10. **References**

Who are Key Personnel?

In the application, we ask you to identify by name pertinent Key Personnel and their specific roles on the project. Key Personnel are defined as (1) the principal investigator or program director; or (2) any other person, including an independent consultant or an employee of a Subcontractor or Partner, who is expected to contribute to the scientific development or execution of the project in a substantive, measurable way *and* who is expected to: (a) receive or has been promised income, or anything else of value, of $10,000 or more per year for his or her contribution to the project or (b) contribute one percent (1%) or more effort to the proposed project. "Key Personnel" does not include a person who is expected to be involved in the proposed project but who does not satisfy conditions (1) or (2).

Individuals who do not meet the definition of Key Personnel may be supported with CIRM funds, but should not be identified by name in the application. Such unnamed personnel may be referenced indirectly by their role on the project (e.g., technician). The budget includes a line item for requesting support for unnamed personnel.

What should one know before preparing the budget?

Budgets must be justified in detail, including all subcontracts and consulting fees, including, if applicable, any additional costs that would be funded from another source. Allowable Project Costs for research funded by CIRM are detailed in the CIRM Grants Administration Policy for Discovery and Translation Stage Programs.

Generally, project costs for personnel, supplies, travel, equipment, and subcontracts may be claimed. Limits for specific cost categories must be observed.

What are Direct Facilities Costs?

Direct Facilities Costs are the general operating costs of the grantee's facilities attributable to housing all elements of the CIRM-funded project or activity. Facilities costs for non-profit applicant organizations are limited to the current applicable, federally negotiated rates for the organization as defined by the Office of Management and Budget (OMB) Circular A-21 or A-122. Facilities rates for for-Profit applicant organizations are limited to 35% of the direct project costs. Facilities rates are applied to direct project costs exclusive of the costs of equipment, tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant, and service agreement in excess of $25,000. The facilities cost rates approved and in place at the time of the application are to be applied to the entire award project period.

How much can an applicant claim for indirect costs?

For-profit organizations cannot claim indirect costs. For non-profit organizations, indirect costs will be limited to 20% of allowable direct research funding costs awarded by CIRM (i.e., project costs and facilities costs), exclusive of the costs of equipment, tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant, and service agreement in excess of $25,000. The indirect cost rate budgeted at the time of application is to be applied to the entire award project period.

Award Administration

Issuance of Award

A CIRM award is issued via a Notice of Grant Award (NGA), which is the formal contract that defines the terms and conditions of an award and documents the commitment of funds from CIRM. CIRM reserves the right to modify or establish funded project activities and the associated budget prior to issuance of the Notice of Grant Award. CIRM also establishes project milestones, success criteria and timelines for milestone achievement at its sole discretion after consultation with the PI and based on information provided in the application. CIRM may also review key contracts/agreements that are critical to the success of the project for compliance with CIRM's policies and regulations.

Payments and Reporting

Upon execution of the NGA, CIRM will issue an initial payment; subsequent disbursements will be made as outlined in the NGA. Continued CIRM funding is contingent upon timely scientific progress against milestones as outlined in the project milestones and timelines established under the NGA. Where project milestones are not timely met, CIRM reserves the right to either redirect resources to maximize the project outcome or, at its sole discretion, to suspend payment and/or terminate the project.

Grantees will be required to provide periodic written progress and financial reports to CIRM. CIRM will partner with the grantee to foster the success of the project. Grantees will have ongoing communication with the CIRM Program Officer

throughout the duration of the award, typically meeting by teleconference and periodically in person.

No-Cost Extensions

Timely progress on funded projects is of crticial importance to CIRM. Therefore, CIRM will consider a one-time, No-Cost Extension (NCE) request of no more than 6 months, submitted at least 30 days before the project end date. Such requests should properly justify how such an extension will advance the project towards its expected outcome, but Grantees should not assume CIRM will approve a NCE request.

Progression Events and Progression Award Application and Administration

Quest Grant Awardees who have achieved a Progression Event within one year of the project end date must submit a Progression Event Report to CIRM to be eligible for a Progression Award. The Progression Event Report will include 1) a description of how the Quest Award candidate will be further developed through translational stage activities and 2) documented evidence of financial support for these follow-on activities, such as a subsequent grant award or venture funding.

A Progression Award proposal must be submitted concomitantly with the Progression Event Report to be reviewed and approved by the CIRM Team. Activities that will be supported by Progression Awards are identical to those of described for DISC 1: Inception Awards, Discovery Stage Research Projects.

Progression Awards will be administered using the mechanism described for CIRM Inception Awards (DISC1). The first payment issued upon initiation of award will comprise 75% of allowable funds. The final 25% will be disbursed upon award closeout including receipt and CIRM approval of final progress and financial reports. No cost extensions for Progression Awards will not be permitted.

Contacts

For information and assistance with this program announcement please contact:

Send email correspondence to Discovery@cirm.ca.gov

or

Call our main line at 510-340-9101 and select "Funding Opportunities" then "Discovery"

CIRM 2.0

CALIFORNIA'S STEM CELL AGENCY

Definitions

"California organization" means: An entity, regardless of profit status, that has >50% of its employees located in, and paid in, the state of California, and conducts the award activities from the California location.

"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. Such organizations also are referred to as "commercial organizations".

"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.

"Partner" means an organization that, in exchange for the right to the opportunity for a future financial return, has (1) agreed to provide matching funds for the proposed project or (2) entered into an agreement with the applicant organization relating to the commercialization of the proposed project.

"Progression Event" means: successful acquisition of funding for the next stage of development of the Quest Award candidate.

"Subcontractor" means an organization (other than the applicant organization) that is expected to: (a) contribute to the scientific development or execution of the project in a substantive, measurable way *and* (b) receive $25,000 or more through the proposed project. "Subcontractor" does not include suppliers of widely available goods.

Appendix

CIRM Regulations

Grant awards made through this PA will be subject to all applicable CIRM regulations. These regulations can be found on CIRM's website.

Target Product Profile

A Target Product Profile (TPP) is a strategic product development tool for therapeutic development that is the subject of a guidance document released by the FDA. Diagnostic, medical device and tool product development more typically employs a development tool often designated as the Product Concept Document (typically includes e.g. an assessment of unmet medical, technical and user needs, competitive and IP assessment, intended use, regulatory path to use, design input). For consistency in our Translation Program we request a TPP, specifically tailored to each candidate type (therapeutic, diagnostic, medical device or tool), which in the case of diagnostic, medical device or tool incorporates elements of the Product Concept Document. A draft TPP template for a candidate that is a therapeutic, a diagnostic, a medical device or a tool may be found within the respective proposal templates for the CIRM Translational Program applications and these templates may be accessed via the following links: TRAN 1, TRAN 2, TRAN 3 and TRAN 4.