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Partnering Opportunity to Create a CIRM Translating Center

INFR 2

REQUEST FOR APPLICATIONS

03.21.16

Partnering Opportunity to Create a CIRM Translating Center

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Objective

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

The objective of this partnering opportunity is to create the CIRM Translating Center, a focused preclinical research organization specializing in stem cell treatments. This organization will support activities related to stem cell process development and manufacture and preclinical research necessary to obtain an Investigational New Drug (IND) application. Operating from a facility permanently located within California, the Translating Center will support CIRM-funded projects but will also be expected to build a sustainable business that will extend the services to other clients in the future.

The Translating Center will coordinate with CIRM's Accelerating Center to deliver its preclinical Core Services to CIRM-funded project teams. The Accelerating Center will act as the lead organization in interactions with the FDA in support of regulatory submissions and, therefore, both centers must work together to support a cohesive development plan for the client. Together, these CIRM Infrastructure Programs will support CIRM-funded translational, preclinical, and clinical projects to develop stem cell treatments for patients with unmet medical needs.

As with the Accelerating Center, the Translating Center is expected to achieve substantial efficiencies by focusing on stem cell treatments. It is important to note that these centers are designed to address common concerns raised by **both researchers and regulatory officials**, making them valuable tools to increase the quality and speed of clinical and translational stage stem cell projects.

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Award Information

What is the CIRM funding allocation and project term?

Under this program, a single applicant organization will be supported to develop and operate the Translating Center within California. The award will provide up to $15M in funding over a five-year period.

What activities must be performed under the CIRM award?

The Translating Center will assist clients with preclinical research services. It must provide the following Core Services for projects developing stem cell treatments under the CIRM award:

- ✓ **Consultation Services:** Provide consultation to clients about appropriate process development and preclinical studies to enable their product development plans and to support competitive applications for CIRM funding.
- ✓ **Project Management**: Initiate, plan, track, and coordinate activities necessary for preclinical IND/IDE-enabling development projects.
- ✓ **Preclinical Development Research**: Conduct preclinical research activities, including pivotal pharmacology and toxicology studies.
- ✓ **Process Development:** Develop cGMP-compatible manufacturing processes suitable for IND/IDE-enabling preclinical studies and to support clinical trial(s) with stem cell and gene modified stem cell products.
- ✓ **Product Manufacturing:** Manufacture stem cell and gene modified stem cell products under cGMP for use in preclinical and clinical studies and, when appropriate, to support successful technology transfer to external manufacturing organizations.
- ✓ **Regulatory Filing Support**: Generate documentation required for filing regulatory applications.

What activities will CIRM not fund?

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

- ✘ Early research and translation for candidate discovery/selection
- ✘ Construction or renovation of physical facilities
- ✘ Activities performed by the Accelerating Center

What are the expected outcomes of the proposed CIRM Translating Center?

The CIRM Translating Center is intended to accelerate clinical development of stem cell treatments to patients by creating a focused preclinical research organization specializing in stem cell products.

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Integration with CIRM Infrastructure Programs. The Translating Center will achieve a coordinated and efficient work-flow with the Accelerating Center to best serve the overarching objective of accelerating stem cell treatments to patients with unmet medical needs. Collectively, these assets are described as Mission Critical Infrastructure in CIRM's Strategic Plan [https://www.cirm.ca.gov/sites/default/files/files/agenda/151217_Agenda_7_CIRM_StratPlan_final_120815.pdf].

The Translating Center Director will serve on a newly formed joint Translating Center/Accelerating Center/CIRM Steering Committee to oversee the coordination of these programs.

Establishment of a Sustainable Business. The Translating Center will develop assets through the aggregation and development of operational improvements and regulatory knowledge gained in supporting cell product development projects. The Translating Center is expected to implement a sustainability plan designed to leverage these assets in the context of CIRM's Infrastructure Programs. The aim is to create a sustainable platform for ongoing acceleration of stem cell treatments to patients.

The Translating Center must utilize the CIRM funding to provide a competitive, reduced rate for services provided to all CIRM-funded projects during the term of the award.

While CIRM funds can only be used for CIRM-funded projects, the Translating Center may charge commercially reasonable fees to support other non-CIRM funded projects. However, the Translating Center may not use CIRM funds to subsidize the direct costs of services provided to non-CIRM funded projects.

This Business and Sustainability plan for the organization must be designed to (i) maximize broad access to clients throughout the state who are developing stem cell treatments, (ii) increase the probability of creating a sustainable business enterprise and (iii) minimize competing interests to support business development.

How will funds be awarded?

CIRM will disburse funds pursuant to a Notice of Award (NOA) and based on operational milestones. **Costs resulting from a delay or failure to meet an operational milestone will be the sole responsibility of the recipient.** Successful applicants will have thoughtfully accounted for foreseeable project risks and developed contingency plans that **do not** require additional funding from CIRM.

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Eligibility

What are the eligibility requirements for partnering with CIRM?

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

(1) Must be ready to initiate work on the funded project within 45 days of approval

Given the urgency of CIRM's mission, the approved awardee must initiate work on the funded project within 45 days of approval and authorization for funding by the Application Review Subcommittee of CIRM's governing board, the Independent Citizens' Oversight Committee ("ICOC").

(2) Must have a California operating location

Applicants must conduct a majority of the Translating Center's operations from a facility permanently located within California that is adequately equipped to provide the required Core Services. The Center Director and a majority of the Center's dedicated staff must work out of the California facility and any effort for which salary is claimed must be expended in California.

(3) Applicants must demonstrate solvency

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

(4) 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 serve as the Center Director (CD)?

To be eligible, the CD 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 100 percent effort to working on the project for the first three years of CIRM-funding and no less than 80 percent effort in years four and five.

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Schedule and Deadlines

Applications Due	2:00 PM PDT, July 15, 2016
Grants Working Group (GWG) Review	Q3/Q4 2016
ICOC Review and Approval	Q3/Q4 2016
Award Start	Must start within 45 days of award approval

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 ensure the submission of high quality applications. 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.

Budget Review

A team of budget professionals will review the proposed budget regarding how the proposed costs compare with established market rates for similar activities (or how well the costs are justified when market rates are not established). When a proposed budget differs significantly from market rates, adjustments to the budget will be required by CIRM prior to further review of the application. Applicants will be notified of the specific discrepancies and applications will not be forwarded for scientific review until an amended budget has been submitted and approved by CIRM. Additionally, project budgets may be subject to further adjustments prior to issuance of an award based upon assessments of the GWG, the CIRM team, or by the Application Review Subcommittee of the ICOC.

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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 at http://www.cirm.ca.gov/WorkingGroup_GrantsReview. The composition of the ICOC can be viewed at http://www.cirm.ca.gov/GoverningBoard.

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. The GWG will score each applications and the highest scoring application will be recommended for funding to the ICOC's Application Review Subcommittee.

The ICOC's Application Review Subcommittee will make final funding decisions giving consideration to the GWG recommendation and any CIRM team recommendation.

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 proposed center hold the necessary significance and potential for impact?

How likely is the proposed center to accelerate the progression of stem cell projects from the late preclinical stage to IND filing and conduct of clinical trials? Does the proposed center offer a sufficient, impactful, and practical value proposition for preclinical researchers, patients, and/or healthcare providers by increasing the speed and quality of preclinical stage stem cell projects?

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2. Has the applicant developed a plan designed to successfully establish and operationalize the center?

How likely is the proposed center to seamlessly integrate with the CIRM Accelerating Center to accelerate CIRM–funded stem cell projects? Is the operation of the center appropriately planned and designed to provide meaningful, accelerating, and impactful resources (including the required Core Services) for the conduct of stem cell preclinical research? Do the project plan and timeline for establishing the center demonstrate an urgency that is commensurate with CIRM's mission? Is an effective plan proposed to provide specialized services that are unique to diverse stem cell and gene modified cell treatments? Is business and sustainability plan appropriate to serve CIRM projects with competitive pricing while ensuring sustainability of the center beyond five years?

3. Is the proposal feasible?

Is the proposed center likely to be established within the proposed timeline? Is the proposed team appropriately qualified and staffed? Does the team have access to all the necessary resources, including necessary collaborations and partnerships, and does their track record support feasibility to establish, equip, operate, and maintain the center? Will the center have the capability and resources to provide the required Core Services? Does the team have a viable contingency plan to manage risks and delays?

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Application Components and Submission

How does one apply?

Applications must be completed and submitted online using the CIRM Grants Management Portal at https://grants.cirm.ca.gov. Any prospective CD must create a login in the system to access application materials and apply. Applications are available in the system only to the CD. A CD may submit only a single application.

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 objectives of the partnering opportunity, provide a detailed plan of proposed activities, complete a detailed budget, and provide reference materials that confirms the status of the project. Applicants will also be required to provide a financial contingency plan that addresses how the applicant will cover possible funding shortfalls.

The main body of the proposal contains the following sections:

1. **Project Summary:** A brief description of the overall project.
2. **Statement of Significance and Impact**: Describe how the core services will serve to accelerate the progression of stem cell projects from the late preclinical stage to IND-filing and conduct of clinical trials and describe the value proposition. Describe the contribution of each Core Service towards:
    a. Accelerating advancement of CIRM projects from the preclinical stage to IND or IDE filing.
    b. Providing a sustainable (beyond the five-year award period) value proposition to preclinical researchers, patients, and/or healthcare providers by improving the speed and quality of the preclinical data package to support regulatory filings for stem cell treatments.
3. **Project Plan**:
    a. Describe how the CIRM Translating Center will seamlessly integrate with the CIRM Accelerating Center to accelerate CIRM-funded stem cell projects.
    b. Describe how Core Services will be provided to achieve the objective of this RFA and how the center will specialize to provide services unique to stem cell treatments.
4. **Operational Plan**: Describe how the Translating Center will be operationalized within proposed timelines to provide meaningful, accelerating and impactful resources for the conduct of stem cell preclinical research.
5. **Business Plan & Sustainability**:
    a. Describe how the Translating Center will provide Core Services meeting the requirements set forth in this RFA to build a business sustainable

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beyond the five-year award period while optimally supporting the CIRM pipeline of projects.

b. Propose a marketing plan that describes how the collective resources and capacities (organizational experience and assets) will be marketed to attract sponsors.

c. Indicate how you propose to utilize CIRM funds to offer competitive services and pricing to CIRM projects.

6. **Timeline**: Provide an activities-based timeline for set up and operations in Gantt chart-like format.

7. **Organizational Experience and Assets**

   a. Describe relevant experience in management and conduct of process development and preclinical IND-enabling Core Service activities
   b. Discuss any specialized assets the applicant brings that may be deployed to accelerate preclinical projects and/or clinical trials involving stem cell and gene modified cell treatments.

8. **Core Service Capacity, Resources, and Environment**: Describe the resources, facilities and infrastructure the applicant will dedicate to each of the Core Services:

   a. **Consultation Services**

   b. **Project Management**

   c. **Preclinical Development Research**

   d. **Process Development**

   e. **Product Manufacturing**

   f. **Regulatory Filing Support**

   For each Core Service, describe the available resources, facilities, and infrastructure and how they will be leveraged to achieve the plan in the timeline provided.

9. **Team Organization**: Describe the team structure, leadership, and communications plan. Describe how the team will coordinate with the Accelerating Center team to best serve sponsors to achieve an IND or IDE filing on an accelerated timeline.

10. **Contingency Plan**: Summary of potential risks, costs associated with those risks, and mitigation strategies, together with a financial contingency plan outlining viable funding sources in the event that costs exceed the amount of funding disbursement.

11. **References:** List all references used in the body of the proposal.

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

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contribute to the technical development or execution of the Translating Center 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?

A specific and well-justified budget must be provided that clearly outlines the total costs of the project, including those costs not proposed to be funded by CIRM. The corresponding budget justification should provide enough detail to allow budget professionals to determine the appropriateness of the costs in relation to the activities being performed. Allowable Project Costs are detailed in the CIRM Grants Administration Policy for Clinical 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 the rules for spending CIRM funds outside of California?

Awardees may use CIRM funds for Allowable Project Activities conducted both in California and outside of California. "Allowable Project Activities" means those activities that are conducted in California and those activities conducted outside of California, provided that: (a) the Awardee exercises direction, supervision and control over the activities and (b) a separate out-of-state organization that performs project activities does not retain intellectual property or publication rights in any intellectual property (e.g., invention, technology, data) arising out of the CIRM funded project.

What are Direct Facilities Costs?

Direct Facilities Costs are the general operating costs of the Awardee'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.

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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.

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Award Administration

Issuance of Award

A CIRM award is issued via a Notice of Award (NOA) Agreement, which is the formal contract that defines the terms and conditions of an award and documents the commitment of funds from CIRM.

Operational Milestones and Payment

CIRM funds under the award will be disbursed based on achievement of specific Operational Milestones established by CIRM. An "Operational Milestone" is an objective event that is indicative of project progress occurring as proposed in the application. CIRM establishes Operational Milestones for inclusion in the Notice of Award based upon information provided in the Application. Upon issuance of the award, funds budgeted to achieve the initial Operational Milestone will be disbursed. Upon the successful completion of the initial Operational Milestone and each successive milestone, additional funds will be disbursed. If funds allocated to a specific Operational Milestone (including both CIRM funds and the required applicant co-funds) are exhausted prior to achievement of that milestone, the Awardee will be responsible for covering any remaining costs. CIRM expects that the applicant's contingency plan will identify project timeline and budget risks and will provide details for covering such costs, including the source of funding. CIRM reserves the right to make adjustments to the timeline for inclusion in the Notice of Award to ensure that funds are appropriately dispersed across Operational Milestones.

Suspension Events

CIRM reserves the right to hold or terminate disbursements if CIRM determines, in its sole discretion, that a Suspension Event has occurred. A "Suspension Event" means a pre-defined condition that triggers a hold of CIRM funding until the suspension event has been resolved, if resolvable. Following a Suspension Event, the Awardee is expected to provide CIRM with a plan to resolve the issue that triggered the Suspension Event. CIRM establishes Suspension Events for inclusion in the Notice of Award based on information provided in the Application.

Reporting

The Awardee will be required to provide periodic written progress and financial reports to CIRM.

CIRM Regulations

The award made pursuant to this RFA will be subject to all applicable CIRM regulations. These regulations can be found on CIRM's website at http://www.cirm.ca.gov/reg/default.asp. The CIRM Grants Administration Policy for Clinical Stage Programs will govern this award.

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Contacts

For information about this RFA or the review process:

Send email correspondence to Infrastructure@cirm.ca.gov

or

Call our main line at 510-340-9101 and select “Funding Opportunities” then “Infrastructure”

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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.

"Operational Milestone" means an objective event that is indicative of project progress occurring as proposed in the application.

"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.

"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.

"Suspension Event" means a pre-defined condition that triggers a hold of CIRM funding until the suspension event has been resolved, if resolvable.