

CONCEPT PLAN FOR THE TRANSLATING CENTER:

Stem Cell Preclinical Research Organization

Objective

The mission of the California Institute for Regenerative Medicine (CIRM) is to accelerate the safe delivery of stem cell treatments to patients with unmet medical needs. A primary strategic theme is to fund the creation of strategic programs that will work in coordination with one another to address key challenges to the progression of therapeutic candidates through the translational and preclinical (IND- enabling) phase and into well conducted stem cell clinical trials.

To address the unique challenges that currently delay the translation of laboratory based stem cell research to high-quality clinical trials, CIRM is proposing two new strategic programs: (1) the Translating Center: Stem Cell Preclinical Research Organization and (2) the Accelerating Center: Stem Cell Clinical Research Organization. These centers are designed to complement each other and work synergistically with one another and the Alpha Clinics Network to support CIRM-funded Translational and Clinical projects. The Translating Center will support activities related to cell process development and manufacturing and preclinical research necessary to obtain an Investigational New Drug (IND) application, which is a prerequisite for clinical testing of cell therapy product candidates, while the Accelerating Center will support IND submissions and clinical trials for these projects.

It is important to note that these two centers are designed to address common concerns raised by **both researchers and regulatory officials**, making them particularly valuable tools to increase the quality and speed of clinical and translational stage projects.

This award will fund the Translating Center, a top quality organization with a proven track record of providing cGMP compliant cellular product process development and manufacturing services and management of preclinical data packages suitable for inclusion in regulatory filings (IND) to support clinical testing of given cell products. Operating from a facility permanently located within California, the Translating Center will provide pre-clinical research services to clients developing cell-based therapeutic candidates, with an initial emphasis on CIRM-funded projects and a business plan to extend the services to other clients in the future. Core services shall include:

- Development of cGMP compliant cell manufacturing processes
- IND-enabling safety and toxicity studies
- Coordination with FDA and the Accelerating Center to support IND filings

The Translating Center will coordinate the delivery of these core services to the sponsors of CIRM-funded projects with CIRM's Accelerating Center. As with the Accelerating Center, the Translating Center is expected to achieve substantial efficiencies by focusing on cell therapy projects.

Award Information

What is the CIRM funding allocation and project term?

Under this program, a single applicant organization will be funded to operate the Translating Center within California. The Translating Center will receive seed funding of up to \$15 million for five years to work in coordination with CIRM's other Strategic Programs to support the filing of an IND.

What activities will CIRM fund under this award?

CIRM will support the following activities under this opportunity:

- ✓ Project planning in coordination with CIRM and the Accelerating Center.
- ✓ Project management for pre-clinical IND-enabling development programs, including pivotal pharmacology and toxicology studies.
- ✓ Process development and product manufacturing activities suitable for production of cell products under good manufacturing practices (GMP).
- ✓ Assembly and authorship of documents to support IND submissions and FDA interactions.
- ✓ Development and execution of a business plan to sustain operations beyond CIRM funding.

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 that are already funded by CIRM under a prior or existing award
- ✗ Activities performed by the Accelerating Center

How will funds be awarded?

CIRM will disburse funds pursuant to a Notice of Grant Award 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** involve additional funding from CIRM.

Project Requirements

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

(2) Must provide core support services

The Translating Center will provide services to optimize translational and clinical programs. Systems and services must include:

- Planning and consultative services related to IND enabling activities
- Process optimization and development for the production of the cell therapy product that ensure compliance with FDA cGMP requirements with accompanying quality systems, technology transfer and scale-up/scale out plans that support future clinical and product development
- Management of standard preclinical safety/toxicity studies that are required for submission of an IND. The Translating Center will not perform animal research but will manage the completion and compilation of the preclinical data package
- Coordination with the Accelerating Center to support IND compilation and submission
- Cell manufacturing and banking and/or assembly of the technology transfer package for cell manufacturing and banking to support clinical trials

Through the development of systems and the provision of the aforementioned services, the Translating Center will obtain unique experience and insight into optimal approaches for performing and accelerating the cell manufacturing and preclinical activities required for obtaining an IND.

(3) Leveraging CIRM's Capacities

The Translating Center will work with the Accelerating Center to best serve the objectives of the two strategic programs and to create an efficient work flow for IND support. The Accelerating Center will serve as the lead organization in interactions with the FDA.

(4) Business and Sustainability Planning

Through the aggregation of process development, manufacturing and related regulatory knowledge, the Translating Center will develop unique information assets. The Translating Center is expected to develop a Sustainability Plan for the deployment of these assets to leverage CIRM's strategic and infrastructure programs. The aim of this leveraging strategy is to create a sustainable platform for ongoing development of stem cell treatments for patients. Systems and planning should:

- Perform ongoing evaluation to align capacity with demand for services.
- Document the market competitiveness of the services provided within this program to support business development.
- Guide the planning and implementation of any "course corrections" emerging from ongoing evaluation activities.

(5) Operational Requirements for the Translating Center

The Translating Center must provide a competitive discount for services provided for all CIRM related activities (current and future CIRM translation and clinical programs and CIRM programs being supported by the Accelerating Center) during the term of the award. The CIRM funds will be used to off-set the costs of providing services supported under this award during the funding

period.

The Translating Center may charge commercially reasonable fees to support other non-CIRM projects. However, the Translating Center must utilize its own funds to provide services to non-CIRM programs.

This organization must be designed to (i) maximize broad access to a clients throughout the state who are developing cellular therapeutics, (ii) increase the probability of creating a sustainable business enterprise and (iii) minimize competing interests.

(6) Participation in Steering Committees

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

(7) 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 services required by this opportunity. The Center Director and a majority of the Center's dedicated staff must work out of the California facility and must be paid within the state.

(8) Organizations must demonstrate solvency

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

Who can apply?

California Based Organizations

California organizations (for-profit and non-profit) may use CIRM funds for eligible project costs incurred both in California and outside California. To qualify as a California organization, the organization must have >50% of its employees located in, and paid in, the state of California, and manage the award activities from the California location.

Non-California Based Organizations

Non-California organizations may also apply; however, CIRM funding can be used only for allowable expenditures incurred within California. Furthermore, non-California based organizations are required to meet the conditions set forth in paragraph 7 ("Must have a California operating location") under "Project Requirements, What are the eligibility requirements for partnering with CIRM".

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
- 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.

Schedule and Deadlines¹

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| Applications Due | 2H2016 |
| Grants Working Group (GWG) Review | 2H2016 |
| ICOC Review and Approval | 2H2016 |
| Award Start | Must start within 45 days of award approval |

¹ This schedule is subject to change by CIRM's President depending upon CIRM's resources and priorities.