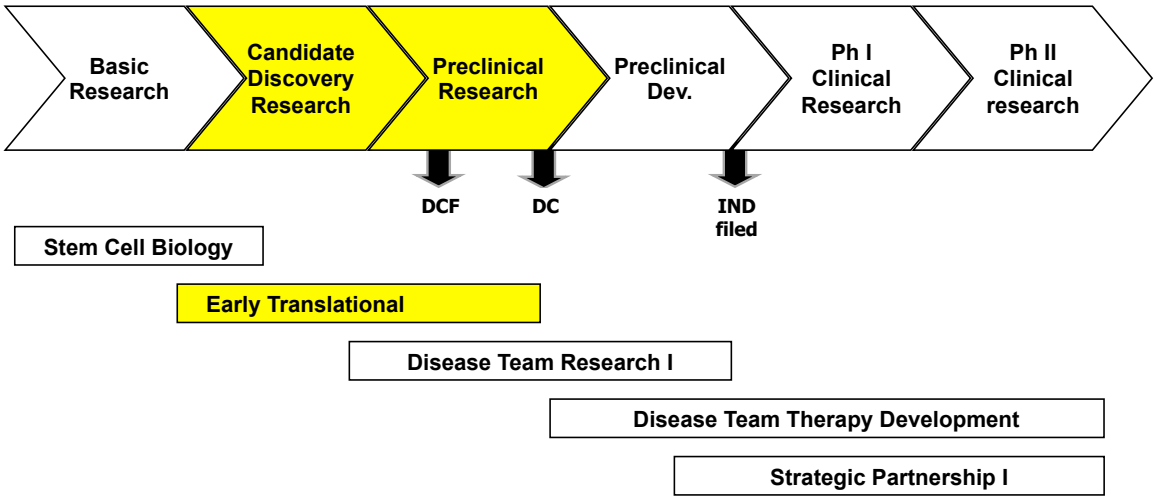
RFA 12-07: CIRM Early Translational IV Research Awards

I. Purpose

The CIRM Early Translational Research Initiative aims to fund and advance stem cell therapies towards IND-enabling preclinical and clinical development. The purpose of this CIRM Early Translational IV Research Awards RFA is the initial translation of promising, innovative stem cell discoveries. This stage of translational research includes the conduct of studies resulting in proof of concept for a potential development candidate and/or studies to select a Development Candidate (DC). The later stages of translational research, including preclinical development and clinical research are supported by other recurring RFAs such as CIRM's Disease Team and Strategic Partnership Initiatives. These recurring translational RFAs are core to our mission to realize the promise of regenerative medicine by enabling stem cell-based therapies, diagnostics and cures for the benefit of patients. The stage of research encompassed by CIRM's Early Translational Program in the context of other CIRM RFAs is highlighted below.



II. Objectives

The objective of the Early Translational IV Research Awards RFA is the conduct of research to achieve either: 1) a Development Candidate (DC award) that could move into IND-enabling preclinical development OR 2) preclinical proof of concept for a potential development candidate. A therapeutic development candidate is a candidate therapeutic entity, suitable for use in humans, which has completed successfully all the necessary research activities to enable initiation of preclinical development activities required for regulatory approval for testing in humans. (See Appendix A for research activities typically required to achieve a therapeutic Development Candidate and that therefore fall within the scope of this RFA.) Similarly, a diagnostic Development Candidate is a candidate diagnostic entity (e.g., a test or assay) that has completed necessary research and is ready to initiate preclinical development activities required for regulatory approval for clinical testing.

A. Award Categories

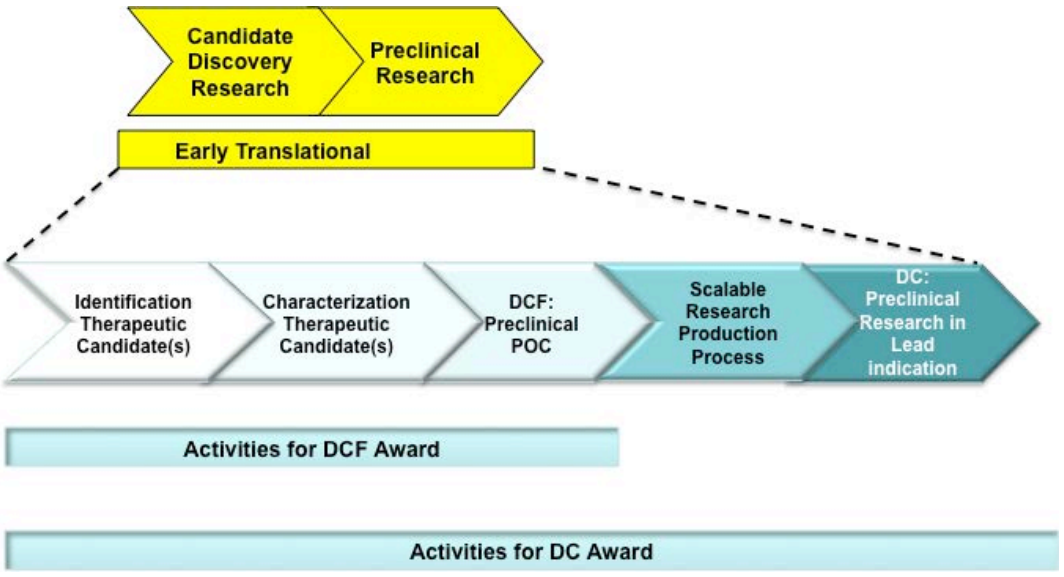
Early Translational IV Research Awards will support two categories of human stem cell/regenerative medicine translational research projects:

1) Development Candidate (DC) Awards: Research that results in a stem cell-derived development candidate (DC) to treat an unmet medical need where all necessary activities to move into IND-enabling preclinical development have been completed.

OR

2) Development Candidate Feasibility (DCF) Awards: Research conducted to identify and/or establish the feasibility of a potential stem cell-derived development candidate. The goal of these development candidate feasibility (DCF) awards is to achieve preclinical (*in vitro/in vivo*) proof of concept for the proposed approach.

These two categories of projects and key research activities are represented below:



By the conclusion of the three-year award period for a Development Candidate Award, a successful therapeutic development candidate must meet the following applicable criteria:

- Suitable for therapeutic use in humans (e.g. not a mouse protein, cell or monoclonal antibody)
- Compatible with applicable regulatory requirements (e.g. GTP, GMP) so it could readily progress into IND-enabling preclinical development. (For example, for a cell therapeutic, the cell line may need to meet donor eligibility requirements and the reagents used in its maintenance should be appropriately sourced and adequately documented)
- Convincing, statistically significant, reproducible disease modifying activity with applicable controls in a relevant preclinical model(s) that is better than standard-of-care therapy
- Preliminary preclinical assessment completed of dose, safety profile (including overt toxicity, immunogenicity and/or genomic integrity, if applicable), therapeutic window, formulation and stability (including genomic stability, if applicable);
- Evidence for potential mechanism of action
- Research assays developed to characterize the candidate (e.g., for identity, purity and activity)
- Methods developed for reproducible and scalable research production of purified candidate (including viral vector, if applicable) at purity, yields and scale adequate to support research and preclinical research studies
- Drug administration mode and method of delivery selected or under development

Comparable relevant criteria must be met at the conclusion of the three-year award period for a Development Candidate Award for a diagnostic candidate. By the conclusion of a Development Candidate Feasibility Award, preclinical proof of concept must be achieved for the therapeutic approach.

Translational research is inherently multidisciplinary, requiring collaboration among scientists with diverse expertise. Thus, in addition to a Principal Investigator, DC Awards may include a Co-Principal Investigator (see section V.C) who brings important complementary expertise to the project. Similarly, to further facilitate collaboration with qualified investigators outside of California who bring important complementary expertise to the project, this RFA is offered as part of our Collaborative Funding Partner Program (see section VI).

B. Responsive Research Activities

The Early Translational IV Research Awards will support research activities that address the criteria listed in the section above (see also Appendix A).

For applications to be responsive to this RFA, one of the following criteria must be met:

- Human stem cells must be necessary to achieve the outcomes of the proposed research.
- Direct reprogramming of human cells is necessary to achieve the outcomes of the proposed research.
- Human endogenous stem cells are convincingly targeted.
- Human cancer stem cells, as defined in below in "Review Criteria", Section X.A.2.a, are convincingly targeted.

For DC Awards, applicants must have already identified a disease/injury target for therapeutic (or diagnostic) intervention.

Examples of responsive research are studies on potential therapeutic development candidates such as stem cells or stem cell-derived progenitor or differentiated cells either genetically modified or not; a biologic or a small molecule with a disease modifying activity on stem cells or their derivatives.

Research that is outside of the scope of these awards and therefore unresponsive includes but is not limited to:
- Basic research and research with a focus on drug target discovery
- IND-enabling preclinical development activities (e.g. GMP production, GLP toxicology and tumorigenicity studies)
- Clinical studies. Analysis of human subject samples, if directly related to the proposed research, can be funded.

C. Award Priorities

In accordance with our mission and key strategic objectives, among responsive proposals, CIRM will prioritize proposals:
- That propose cell therapies, especially cell therapies that are differentiated derivatives of pluripotent stem cells (especially for DC awards)
- That establish proof of concept (DCF awards) for potentially transformative regenerative approaches to unmet medical needs. Rather than representing incremental advances, these new opportunities for regenerative medicine are potentially high impact and paradigm shifting (e.g. direct in vivo reprogramming, tissue engineering approaches).
- That target disease conditions prevalent in neonatal or juvenile patients such as cerebral palsy, schizophrenia or autism spectrum disorders
- That are ineligible for, or unlikely to receive, timely or sufficient federal funding

As CIRM now has a significant translational portfolio, a project proposing a substantially comparable approach/intervention that is already represented in CIRM's translational portfolio (see Appendix B) must be compelling.

In addition, CIRM is supportive of applications from applicants in partnership with a multinational biopharmaceutical company ("Translation Partner") that can accelerate

the project by providing co-funding and product discovery/development expertise and if successful, follow-on product development.

III. Award Information

Under this Request for Applications (RFA), CIRM intends to commit up to $70 million to support the Early Translational Research Awards IV program. Projects will be funded for up to 3 years. Two award types are available:

1. Development Candidate (DC) Awards, each with justifiable total direct project costs of up to $3.5 million over the three-year project period. Direct project costs should be allocated over the project period to best achieve the project objective. CIRM intends to support approximately 10 DC Award projects.

2. Development Candidate Feasibility (DCF) Awards, each with justifiable total direct project costs of up to $1.2 million over the three-year project period. CIRM intends to support approximately 10 DCF Awards projects.

For all awards, CIRM reserves the right to negotiate funded project activities, milestones (both technical and financial), success criteria, timelines and budgets prior to issuance of the Notice of Grant Award (NGA) or Notice of Loan Award (NLA), subject to renegotiation annually and/or based on progress. CIRM may also wish to review (for compliance with CIRM's policies and regulations) key contract/agreements that are critical to the success of the project (e.g. MTAs for cell lines or genes, agreements with Contract Research Organizations, CROs or Contract Manufacturing Organizations, CMOs).

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

Progress in translational research is important to CIRM. Continued funding is contingent upon timely scientific progress as outlined in the project milestones and timeline established under the NGA or NLA. Where milestones are not met, CIRM reserves the right to negotiate new milestones to refocus/redirect the project or to terminate the project. For Early Translational IV Research Awards, CIRM will require a written semi-annual progress report in addition to the annual progress report that is required by the CIRM Grants Administration Policy (GAP, section XV.A).

IV. Award Mechanism

CIRM expects to fund approved proposals from non-profit and for-profit institutions (separately or in collaborations), through grants or loans.

The following outlines the applicable award mechanism:

- For-profit organizations may elect to receive loans for award amounts of $3 million or greater. The loan holder will be responsible for the entire award from CIRM, even if a Co-PI is from a non-profit organization. Loan terms are described in Appendix C.

- Grant, if PI is from a non-profit organization. For-profit organizations may also elect grants.

Grant Terms: Non-profit institutions or PIs at a non-profit organizations will receive grant funding in quarterly disbursements, and be 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.).

Loan Terms: The terms of the Loans are set forth in detail in Appendix C to this RFA. Loan recipients shall be governed by the CIRM Loan Administration Policy that is in effect as of the date of the execution of the Notice of Loan Award. Approved for-profit applicants who accept a loan will pay for loan administration costs out of indirect costs included in the award. Loans are also subject to certain intellectual property requirements as described in 17 Cal. Code Regs. § 100801.

Loan applicants will be required to submit financial information. For information on the loan program, consult the Interim CIRM Loan Administration Policy, available at: http://www.cirm.ca.gov/cirm-operations/Regulations.

V. Eligibility

A. Institutional Eligibility

Both non-profit and for-profit organizations are welcome to apply. At the time of the preliminary application (PreApp) deadline, the applicant organization must be located in California (that is, the organization must have employees who are conducting business or operations at a location in California). At the time of funding, 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 and for-profit institutions sponsoring Co-Principal Investigators (Section V.C, Co-Principal Investigators) are subject to the same eligibility requirements as applicant institutions.

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

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 PreApp 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

In order to broaden the pool of applicants engaged in stem cell research and to encourage leveraging of CIRM’s investment, CIRM is limiting the number of active CIRM research awards in which an investigator may participate as PI or Co-PI. This RFA is not open to investigators as a PI or Co-PI who are already a PI or Co-PI on 3 or more active CIRM awards as of March 20, 2013, the deadline for submission of the full application.

The limit includes all CIRM awards that have been approved but not yet closed out, with the exception of the following CIRM RFAs/PAs: Shared Research Labs, Major Facilities, Research Training Awards I & II, Bridges to Stem Cell Research, Disease Team Planning Awards, Disease Team Therapy Development Part I Planning Awards, or Conference Grants.

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

Translational research is inherently a multidisciplinary effort. CIRM will therefore allow designation of a single CIRM-funded Co-Principal Investigator (Co-PI) ONLY for DC awards. The Co-PI must have an M.D., Ph.D. or equivalent degree and must be sponsored by the institution at which the Co-PI will conduct the proposed research in California.

By the PreApp deadline, the Co-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

Designating Co-PIs is not a requirement. The decision of whether to include Co-PIs (or a Partner PI funded by a CFP, see Section VI) should be guided by the scientific goals of the project.

D. Other Eligibility

The research project and PI (Co-PI and/or Partner PI, if applicable) proposed in the full Application must be the same as that described in the Preliminary Application (Section VIII).

E. Percent Effort Requirements

CIRM, mindful of the urgency of its mission, will only fund PIs and Co-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, 15% for Co-PIs.

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 XV.A of this RFA) and the Loan Administration Policy (see Appendix C 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. Applicants who will need an exception are strongly encouraged to request it at least 30 days before the relevant application deadline. To request an exception, or for assistance in determining whether one is necessary, contact the CIRM staff listed in Section XIV.

VI. Collaborative Funding Partners

CIRM has established a program with several other agencies that fund stem cell and regenerative medicine research. Through this Collaborative Funding Partner (CFP) program, California-based Principal Investigators (PIs) can collaborate with a Funding Partner PI ("Partner PI") from a Funding Partner applicant institution ("partner applicant institution") eligible for funding from one of CIRM's CFPs to bring

important additional resources to the project. If a collaboratively funded proposal is approved (a "CIRM/CFP Award") CIRM will fund all project work done within the State of California and the CFP will fund all project work within its jurisdiction. For this RFA, NIH (US), MOST/Tonji (China), BMBF (Germany) and InStem (India) are participating as CFPs.

To apply for a collaboratively funded project involving CIRM and a CFP, applicants must satisfy both the CIRM requirements and any additional requirements put forth by the CFP. For more details on these requirements, please see Appendices D-H.

Before funding contracts are signed, successful CIRM/CFP applicant teams must have a signed written agreement adequately addressing Intellectual Property (IP) issues relating to the collaborative project and must provide CIRM and the CFP (as required) with copies. These IP Agreements will be reviewed by both CIRM and the respective CFP to ensure that they are consistent with CIRM's applicable IP regulations and with the Agreement between the co-funders.

Before funding contracts are signed, successful CIRM/CFP applicant teams must obtain all necessary approvals for animal protection, human subject protection, and use of human embryonic stem cells, unless the approval is not required to initiate the award. CIRM and the CFP will monitor compliance with approval procedures required in their respective jurisdictions.

Both CIRM and the CFP may be involved in the management/oversight of the CIRM/CFP Award, 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.

VII. Notification Regarding Disclosure Information

All applicants, including those not applying with a Partner PI are hereby notified that CIRM may share Preliminary Applications, full Applications and related information submitted by applicants with a CFP in order to facilitate their participation in this RFA. Information concerning approved CIRM/CFP Awards may also be shared with a CFP. Before receiving any such material, the CFP will agree in writing to hold the materials in strict confidence and to use them solely for purposes directly related to this RFA.

VIII. Application and Evaluation Process

Submission of an application for this RFA involves a two-step process. Any qualified applicant may submit a single, brief Preliminary Application (PreApp). Applicants submitting the most promising, competitive and responsive PreApp proposals will be invited to submit a detailed, full Application. All other applicants will be deferred with the opportunity to apply in response to a future RFA. CIRM expects to reissue an Early Translational Research Awards RFA in approximately 12-18 months.

PreApps should emphasize the overall impact of the proposed work and address the review criteria for the PreApp described in Section X. PreApps will be evaluated by scientific specialists from outside California who are experts in specific areas of research described in the PreApp and by CIRM scientific staff, based on the scientific review criteria described in Section X below. The research project and PI, (Co-PI and/or Partner PI, if applicable) proposed in the full Application must be the same as that described in the PreApp.

Full Applications will be evaluated by the CIRM Grants Working Group (GWG), which is composed of fifteen scientific experts from outside California, seven patient advocate members of CIRM's Governing Board, and the Chair of the Governing Board. The list of scientific members who may participate in the GWG review can be found at http://www.cirm.ca.gov/GrantsWkgGrpMembers. The composition of the ICOC can be viewed at http://www.cirm.ca.gov/GoverningBoard. The fifteen participating scientists on the GWG will review the applications and score them according to scientific and technical merit applying the review criteria described in Section X below. The GWG (scientists and patient advocates) will then review the entire portfolio of applications, taking into consideration the following criteria:

- Appropriate balance among applications that address the priorities of this RFA and other meritorious applications. **CIRM's priorities for this RFA are for meritorious applications that**:
    - Propose cell therapies, especially cell therapies that are differentiated derivatives of pluripotent stem cells (especially DC awards)
    - Propose potentially transformative, rather than incremental, therapeutic approaches to regenerative medicine (especially DCF awards)
    - Address disease conditions prevalent in neonatal or juvenile patients such as cerebral palsy, schizophrenia or autism spectrum disorders
- Appropriate balance among DC and DCF applications
- Appropriate balance in the context of CIRM's translational portfolio (See Appendix B) in order to reduce risk
- Other considerations from the perspective of patient advocates

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. (Per Gov. Code §6254.5(e). Non-public records may be disclosed to government agencies under confidentiality agreements.

IX. Resources for Applicants

In order to facilitate preparation of high quality applications, CIRM advises applicants to take advantage of the relevant translational resources compiled by CIRM. Multiple relevant resources such as joint CIRM-FDA outreach webinars (addressing product characterization, preclinical considerations for cell therapies, imaging technologies for cell therapies, scaffolding and therapies for the eye) as well as Regulatory Resources and FDA guidances, can be accessed through the CIRM website at:

http://www.cirm.ca.gov/RegenerativeMedicineConsortium

and

http://www.cirm.ca.gov/our-funding/resources-researchers/stem-cell-research-resources

In addition, applicants are encouraged to consult Appendix A of this RFA for a list of in scope activities as well as sample, fictitious milestones and success criteria.

X. Review Criteria

CIRM intends the Early Translational IV Research Awards to support research to achieve either a development candidate (DC award) that could move into IND-enabling preclinical development OR establish preclinical proof of concept for a potential development candidate (DCF award). In alignment with our mission, CIRM will ask the reviewers to give added consideration to projects that:

- Propose cell therapies, especially cell therapies that are differentiated derivatives of human pluripotent stem cells (especially for DC awards)
- Address potentially transformative, rather than incremental, regenerative approaches to unmet medical needs. Rather than representing incremental advances, these approaches are potentially high impact and paradigm shifting opportunities for regenerative medicine (especially for DCF awards)
- Address disease conditions prevalent in neonatal or juvenile patients such as cerebral palsy, schizophrenia or autism spectrum disorders

A. Preliminary Application

For both award categories (DC and DCF awards) the PreApp will be evaluated in four key areas: 1) Target Product Profile (TPP), Rationale and Significance, 2) Feasibility and Design, 3) Qualifications of the PI (Co-PI, Partner PI, if applicable) and 4) Responsiveness to the RFA. For Pre-Applications with a Partner-PI, consider the relevant "Partner PI Role" section when evaluating these key areas.

1. TPP, Rationale and Significance:

a. Target Product Profile (TPP): The target product profile is scientifically and clinically reasonable and presents the key attributes of the propose development candidate/intervention.

b. Objective: The objective of the proposed research includes achieving either: 1) a development candidate (DC award) that could move into IND-enabling preclinical development OR 2) preclinical proof of concept for a potential development candidate (DCF award).

c. Scientific rationale: The scientific rationale for the target for intervention and the approach are logical and compelling.

d. Significance:

- The proposed development candidate/intervention addresses an unmet medical need that, if successfully developed and made available to patients, will be a significant improvement to the current standard of care and could have a broad and significant impact on disease, injury or medical practice.
- The proposed approach (DCF awards) is an opportunity to have a transformative, rather than incremental, impact upon regenerative medicine (e.g. direct in vivo reprogramming, tissue engineering strategies).
- The participation in the project of an applicant in partnership with a multinational biopharmaceutical company ("Translation Partner") can accelerate the project and enhance the potential for follow on development and ultimately, patient benefit.

2. Feasibility and Design:

a. Preliminary Results:

The preliminary results are compelling and supportive of the proposed research. For proposals targeting cancer stem cells the cells targeted in the pre-application have been convincingly demonstrated to be cancer stem cells based on the following criteria. Cancer stem cells are self renewing cells of the tumor/cancer, whose identified phenotype can be shown to seed themselves and all the cells of the tumor in two consecutive serial xenotransplants into immunodeficient recipients, as distinct from lack of cancer seeding properties of the non-cancer stem cells of the tumor. Relative enrichment of the cancer stem cell population should be demonstrated by graded cell numbers transplanted or by limiting dilution transplants.

b. Research Plan:

- The research plan is focused, well designed and supports the feasibility of achieving the RFA and project objective within three years.
- The project milestones address all key activities necessary to achieve the objective within three years and are feasible, focused, complete and logical. Examples of milestones can be found in Appendix A.

- The research plan, in conjunction with the preliminary results, is complete such that all the activities required to achieve the milestones and objective are addressed.

3. Qualifications of the PI (Co-PI and Partner PI if applicable):

The PI, and if applicable, the Co-PI and Partner PI have relevant translational research experience, have demonstrated successful leadership experience and have made direct contributions to the preliminary results for the proposed project. For DC awards, the PI has product development experience.

4. Responsiveness to the RFA:

- The proposed research addresses the RFA's objectives.
- Activities proposed are within the scope defined for the RFA as outlined in Section II.B and Appendix A.
- One of the following criteria is met:
    - Human stem cells are necessary to achieve the outcomes of the proposed research.
    - Direct reprogramming of human cells is necessary to achieve the outcomes of the proposed research.
    - Human endogenous stem cells are convincingly targeted.
    - Human cancer stem cells, as defined above in section X.A.2.a, are convincingly targeted.
- For DC awards, a target for intervention for disease/injury has been identified.
- The proposed approach or intervention is novel – if the proposed approach/intervention is already represented in CIRM's translational portfolio (Appendix B), there must be a compelling reason to fund a substantially comparable additional project.

B. Full Application

The full Application will be evaluated in six key areas: 1) Objective and Milestones, 2) Rationale and Significance, 3) Feasibility and Design, 4) Qualifications of the PI (Co-PI, Partner PI, if applicable) and Research Team, 5) Collaborations, Assets, Resources and Environment, and 6) Responsiveness to the RFA. The specific criteria for review of applications are based on the standard review criteria described in the CIRM Grants Administration Policy (GAP, see section XV.A of this RFA).

1. Objective and Milestones:

a. Objective: The objective of the research proposed under the award is defined as achieving either: 1) a development candidate (DC award) that could move into IND-enabling preclinical development OR 2) preclinical proof of concept for a potential development candidate (DCF award).

b. The Target Product Profile (TPP): The Target Product Profile is scientifically and clinically reasonable and presents the key aspirational attributes of the proposed development candidate/intervention.

c. Milestones: The project milestones address all key activities to achieve either preclinical proof of concept (DCF award) or a development candidate (DC award) within three years and are feasible, focused, complete and logical. The proposed success criteria for each milestone provide quantifiable, scientifically and clinically meaningful measure(s) of outcomes for all key activities to achieve the RFA and project objective. Examples of milestones and success criteria can be found in Appendix A.

2. Rationale and Significance:

a. Scientific rationale: The scientific rationale for the target for intervention and the approach are logical and compelling.

b. Significance: The proposed development candidate/intervention addresses an unmet medical need that, if successfully developed and made available to patients, will be a significant improvement to the current standard of care and could have a broad and significant impact on disease, injury or medical practice. Taking into account other treatments in clinical trials, the proposed approach is an opportunity to have a transformative, rather than incremental, impact upon regenerative medicine (especially for DCF awards).

3. Feasibility and Design:

a. Preliminary Data:
The preliminary data are compelling and supportive of the proposed research. The preliminary data are compelling and supportive of successful application of proposed key technologies/methodologies. For proposals targeting cancer stem cells, the cells targeted in the application have been convincingly demonstrated to be cancer stem cells (see Section X.A.2.a for criteria).

b. Research Plan:
The research plan is focused, well designed and supports the feasibility of achieving the milestones and objective within three years. The research plan is complete such that, in conjunction with the preliminary data, all the activities required to achieve the milestones and objective are addressed (e.g. assay development, candidate characterization, preliminary dosing, robust disease modifying activity, MOA, pilot safety). The research plan identifies and acknowledges potential problems, and suggests alternative approaches should the proposed primary approaches fail. All proposed activities are within scope of the RFA and are necessary to achieve the application's objectives. The project timeline, defined by the milestones, is feasible and can be reasonably achieved within the 3-year award period. Assuming success,

there is a reasonable plan for funding and moving the project forward into IND-enabling preclinical and clinical development.

4. Qualifications of the PI (Co-PI, Partner PI, if applicable) and Research Team:

a. Expertise and Experience: The PI (Co-PI, Partner PI, if applicable) has the expertise and relevant translational experience to conduct the proposed research and have directly contributed to the preliminary data. For DC awards, the PI has product development experience.

b. Track Record: The PI (Co-PI and Partner PI, if applicable) has a record of achievement and successful leadership that supports his/her qualifications to conduct and lead the proposed translational research project. If applicable, past performance of the PI, or Co-PI on CIRM awards, should be considered.

c. Appropriate Team: The PI has assembled an appropriate multidisciplinary research team to best achieve the project's milestones and objective. There are experts on the team for all key functional areas.

d. Team Communication: The PI has a reasonable plan for communication, coordination and collaboration among members of the team.

e. Commitment: The PI's (Co-PI's and/or Partner PI's, if applicable) level of commitment to the proposed research increases the probability of successful and timely completion of the project.

f. Appropriate Budget: The budget is focused and appropriate for the research necessary to achieve the project objective(s). For DC Awards, all activities necessary to achieve a development candidate are addressed in the budget.

5. Collaborations, Assets, Resources and Environment:

a. Collaborations: Proposed collaborations (including, if applicable, those with a Co-PI, Partner PI and/or Translation Partner) are critical and integral to the success of the proposed project. These collaborations have been secured and evidence is presented that the collaborator is committed to the proposed research.

b. Relevant Assets: Relevant assets (i.e. intellectual property, licenses) are available to the project. When proprietary cell lines, small molecules, antibodies or other critical materials are required for the project, the applicant has either provided material transfer agreements (MTAs), licensing agreements or appropriate letters of commitment from the asset owner.

c. Resources and Environment: Resources critical to the success of the project, including necessary facilities, major equipment, and services (through advisors, subcontractors) are available for conducting the proposed research. The

environment facilitates the interactions that enhance the probability of success of the proposed research.

d. Institutional Support: The applicant institution is committed to supporting translational research. (Include the Co-PI and/or Partner PI applicant institution(s), if applicable).

6. Responsiveness to the RFA:

- The proposed research addresses the RFA's objectives.
- Activities proposed are within the scope defined for the RFA as outlined in Section II and Appendix A.
- One of the following criteria is met:
    - Human stem cells are necessary to achieve the outcomes of the proposed research.
    - Direct reprogramming of human cells is necessary to achieve the outcomes of the proposed research.
    - Human endogenous stem cells are convincingly targeted.
    - Human cancer stem cells, as defined above in this section under "Preliminary Data" (section X.A.2.a), are convincingly targeted.
- For DC awards, a target for intervention for disease/injury has been identified.
- The proposed approach or intervention is novel – if the proposed approach/intervention is already represented in CIRM's translational portfolio (Appendix B), there must be a compelling reason to fund a substantially comparable additional project.
- Whether and to what extent the 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.

XI. Application Procedure

Applicants must follow these instructions for submission of a PreApp and, if invited, a full Application for the CIRM Early Translational IV Research Awards RFA. Full applications will only be accepted from applicants who 1) submitted a PreApp and 2) are invited by CIRM to submit a full application.

A. Preliminary Application Forms

Each applicant must submit a PreApp using the forms and instructions provided in the Grants Management Portal at https://grants.cirm.ca.gov. A PI may submit only one Pre-App under this RFA.

The PreApp consists of the following sections:

1. Principal Investigator
Identification information about the PI, Co-PI (if applicable), and Authorized Organizational Official. For CIRM/CFP collaborations, include the name of the Partner PI and the Partner applicant institution.

2. Key Collaborators
If key collaborators critical to the project (including co-investigators, Translation Partners or consultants) will be identified and their roles described in the PreApp, use this section to identify up to five such individuals and their respective institutions. For conflict of interest reasons, do not name or identify any additional individuals anywhere in the PreApp.

3. Title of Proposed Project (limited to 90 characters)

4. Target Product Profile (limited to 600 characters for each component)
Provide a target product profile (TPP) for the proposed novel development candidate/intervention. The TPP becomes the product (i.e., drug) label upon commercialization. It therefore guides preclinical and clinical research and development and is continually refined. The TPP should reflect the key attributes known or required/desired for the proposed development candidate/intervention. A draft guidance document from the FDA on the TPP can be found at: www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm080593.pdf. Briefly address each of the following components of a TPP: a) Description of the proposed development candidate/intervention, b) Proposed Disease/Injury indication, c) Desired Activity (in vitro/in vivo), d) Desired Safety Profile, and e) Desired Dose, Route and Regimen. Provide comparable information for a diagnostic candidate.

5. Objective (limited to 1000 characters)
State and explain the objective of the research proposed in the application.

6. Rationale, Significance and Responsiveness (limited to 1500 characters)
Describe the scientific rationale for the target for intervention and for the proposed approach. Justify how the proposed approach will be a significant improvement to the current standard of care and could have a broad and significant impact on disease, injury or medical practice. Address how the proposed approach could advance the field of stem-cell based/regenerative medicine; for DCF awards, justify how the proposed approach could potentially have a transformative, rather than incremental, impact upon regenerative medicine. If applicable, briefly describe the financial and resource commitment of the multinational biopharmaceutical partner company “Translation Partner” to the proposed program and to follow on development of the successful DC. Address how the proposed research meets one of the following criteria:

- Human stem cells are necessary to achieve the outcomes of the proposed research.

- Direct reprogramming of human cells is necessary to achieve the outcomes of the proposed research.
- Human endogenous stem cells are convincingly targeted.
- Human cancer stem cells, as defined in section X.A.2.a, are convincingly targeted.

If the proposed development candidate/intervention is already represented in CIRM's current Translation Portfolio, (see Appendix B), justify why the proposed research would be a compelling addition.

7. Preliminary Results (limited to 3000 characters)

Summarize the preliminary results and other (e.g. published) results that support the proposed research to achieve a development candidate/proof of concept for intervention. For approaches targeting cancer stem cells, provide convincing evidence that cancer stem cells are targeted as described above in the Review Criteria, Section X.A.2.a. Figures or tables cannot be included in the PreApp.

8. Milestones (up to 6 milestones, 500 characters per milestone)

List and describe two to six major milestones of the research to establish the key requirements to achieve a preclinical proof of concept (DCF award) or a development candidate (DC award) within three years. Milestones should consist of measureable assessments of progress, rather merely than tasks to be performed. Please see Appendix A for sample milestones. Indicate the time in the award period when each milestone is to be achieved.

9. Research Plan (limited to 6000 characters)

Describe concisely the research plan and address all the activities required to achieve the project objective and milestones within three years. See section II.A for key DC and DCF award activities as well as DC achievement criteria.

10. Qualifications of the PI (Co-PI, Partner PI) (limited to 2000 characters)

Describe the qualifications of the PI and if applicable, the Co-PI, Partner PI to lead and conduct the proposed research. Highlight translational research leadership and experience. For DC awards, describe the PI's product development experience.

11 Project Keywords

Select one keyword in each category (from the list provided) that best describes the proposed research. If appropriate, supply additional keywords that are central to the proposed project.

12. Partner PI Role Information (limited to ~3000 characters)

If applicable, elaborate on the role of a Partner PI towards the proposed program, including preliminary data contributions, activities to be conducted as part of the research plan and responsibility for achieving the proposed milestones.

13. Related Business Entities Disclosure

Applicants must complete the Related Business Entities Disclosure section, when applicable (see instructions at https://grants.cirm.ca.gov). Applicants (PIs) from a for-profit institution, including Co-PIs and Partner PIs from a for-profit institution to be funded by the Funding Partner) must complete the form by listing all related business entities. The information in this form is required for compliance with the Conflict of Interest policy under which CIRM operates. If named in the PreApp, a Translation Partner company participating in the proposed project should also be listed in this section.

B. Preliminary Application Submission Instructions

PreApps must be submitted online using the CIRM Grants Management Portal at https://grants.cirm.ca.gov. A PI may submit only a single PreApp for this RFA and it must be received by CIRM no later than 5:00 pm (PDT) on October 26, 2012.

C. Full Application Forms

Full Applications for this RFA may be submitted only by applicants who 1) submitted a PreApp (as described above) and 2) are invited by CIRM to submit a full Application. Application forms will be available via the Grants Management Portal at https://grants.cirm.ca.gov in January 2013.

The application for the CIRM Early Translational IV Research Awards RFA consists of **five parts**:

Part A: Application Information Form (Web-based form)
Part B: Proposal (MS Word template)
Part C: Biographical Sketches (MS Word template) **and Letters of Collaboration/Support**
Part D: Licenses and Agreements (e.g. MTAs). If you have licenses or MTAs in place, submit copies. For applicants who have a Translation Partner, submit documentation on the partnership (e.g. Letter of Intent, Partnership Agreement.
Part E: Budget Detail (MS Excel template)

The full Application includes the following sections:

1. Abstract (up to 1500 characters in Part A)
State the objective and provide a brief description of the proposed research. Summarize the rationale for the target for intervention and for the proposed approach. Describe the unmet medical need that the proposed development candidate/intervention will address. Summarize the significance that the proposed research could have on the treatment of disease or injury, if it were successfully developed. Summarize the proposed research plan focusing on key research activities to be achieved within any given budget year. Summarize the milestones to be achieved within any given budget year.

2. Public Abstract (up to 1500 characters in Part A)
In lay language, briefly describe the proposed research and how it will achieve either a development candidate or preclinical proof of concept for a potential development candidate that could advance the use of stem cells for therapy. This Public Abstract will become public information and will be available online; therefore, DO NOT include proprietary or confidential information or information that could identify the applicant (e.g., PI name, applicant institution name or location) and, if applicable, the Co-PI, the Partner PI, the Translation Partner and their respective applicant institutions.

3. Statement of Benefit to California (up to 1500 characters in Part A)
Describe in a few sentences how the proposed research will benefit the State of California and its citizens. This Statement of Benefit will become public information and will be available online; therefore, DO NOT include proprietary or confidential information or information that could identify applicant (e.g., PI name, applicant institution name or location) and, if applicable, the Co-PI, the Partner PI, the Translation Partner and their respective applicant institutions.

4. Key Personnel (included in Part A and C)
List all key personnel and their roles on the project in the appropriate sections of Part A. Key personnel are defined as individuals who contribute to the scientific development or execution of the project in a substantive, measurable way, whether or not they receive salaries or compensation under the grant. Key personnel may include any co-investigators, collaborators, consultants, technical staff or trainees, who meet this definition. Key personnel who are not part of the applicant (or co-applicant) organization should be listed in the subcontract section of the application. Personnel that are not key, such as technical support staff, may be supported by grant funds but not named.

For Development Candidate Award applications that designate a CIRM-funded Co-PI, key personnel sponsored by the Co-PI must be listed in Part A. Where the Co-PI is employed by an institution other than the applicant institution, key personnel for the PI can include a project financial administrator. For CIRM/CFP applications, key personnel sponsored by the CFP, their contributions to and percent effort towards the project must also be listed in the corresponding section of Part A.

A minimum of one percent effort is required for each key person, except the PI, who is required to commit a minimum of 20% effort, and Co-PI who must commit a minimum of 15% effort.

For each key person listed, provide a two-page biographical sketch using the template provided under Part C. The sketch should highlight prior relevant translational research and product development experience, accomplishments and/or special skills related to the proposed research. Include relevant publications and/or patents or patent applications. Following biographical

sketches for the PI and, if applicable, the Co-PI, Partner PI and/or Translation Partner lead, include all remaining biographical sketches in alphabetical order.

5. Budget (included in Parts A and E)

Provide all budget information requested in the budget section of Parts A and E. Budgets must be justified in detail, including all subcontracts and consulting fees. For Development Candidate Award applications that designate a Co-PI, the PI and the Co-PI will each be responsible for an individual budget (comprised of CIRM Direct Project Costs, CIRM Direct Facilities Costs and CIRM Indirect Costs) for that portion of the total project performed under their authority. For CIRM/CFP collaborations, the funding requested from the CFP (total and per year requested, Part A) must be indicated and justified in sufficient detail (in the Part A section "Budget Justification") for reviewers to assess the appropriateness of the non-California research budget. Similarly, for CIRM/Translation Partner collaborations, the matching funds provided by the Translation Partner (total and per year requested, Part A) must be indicated and justified in sufficient detail (in the Part A section "Budget Justification") for reviewers to assess the partner's contribution to the project.

If, to achieve the objective of the project described in Part B, the applicant will require funding from sources other than those listed above, then the applicant must specify and justify the added cost and identify funding sources that will enable conduct of the project (in the Part A section "Budget Justification").

All allowable costs for research funded by CIRM are detailed in the CIRM Grants Administration Policy (GAP, see Section XV.A of this RFA). For CIRM/CFP teams, allowable costs for research funded by the Collaborative Funding Partner may differ. Guidance will be provided separately by NIH (US), MOST/Tonji (China), BMBF (Germany) and InStem (India) in appendices D-H, respectively.

Under this RFA, CIRM-funded allowable costs include the following:

- ***Salaries for Key Personnel***
  Salaries for Key Personnel may include the Principal Investigator, Co-Investigators, Research Associates, and technical support staff, each of whom must perform the subject work in California, based on percent of full time effort commensurate with the established salary structure of the applicant institution. The total salary requested must be based on a full-time, 12-month staff appointment or the full time annual salary for employees of a for-profit institution. Institutions may request stipend, health insurance and allowable tuition and fees as costs for trainees. With the exception of the project financial administrator for projects where a Co-PI is at an institution other than that of the PI, administrative support salaries should be covered exclusively by allowed Indirect Costs.

• Supplies
Grant funds will support supplies, including specialized reagents and animal costs. Minor equipment purchases (less than $5,000 per item) are considered supplies and may be included as direct costs in the budget.

• Travel
Recipients (PIs) of CIRM Early Translational IV Research Awards are encouraged to attend a CIRM-organized grantee meeting in California and should include travel costs for this meeting in the budget. Travel costs associated with collaborations necessary to the grant are allowable. Details of allowable travel costs can be found in the GAP (see Section XV.A of this RFA).

• Equipment
Major equipment (more than $5,000 per item) necessary for conducting the proposed research at the applicant institution should be itemized and justified. Under this RFA, no more than 5% of total direct project costs can be used for equipment. Under special circumstances, with sufficient rationale, CIRM may allow a higher percentage of direct project costs for equipment. Equipment costs should not be included as allowable direct costs in indirect cost calculations.

• Consultants/Subcontracts
Grantees that subcontract CIRM-funded work should note that CIRM-funded **research** must generally be conducted in California.

Aside from small consulting contracts, Grantees may not use CIRM funds to contract for research to be performed outside of California. Consulting contracts for out-of-state research are limited to $15,000 per year for a single contract, and $25,000 per year in aggregate. (CIRM may allow modest increases to these limits in exceptional circumstances.)

For activities **other than research**, Grantees may subcontract outside California, but must make a good faith effort to use California suppliers for more than half of their contracts and purchases in accordance with CIRM's California Supplier regulation (Cal. Code Regs., tit. 17, § 100502). Examples of such activities include generation of a cell line/research cell bank that is GMP compatible and humanizing a lead murine monoclonal antibody performed according to an existing, standard protocol.

•Facilities Costs
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%. Facilities rates are applied to direct project costs exclusive of the costs of equipment, tuition and fees and subcontract amounts in excess of $25,000. Applicants may use

lower Facilities rates, and use up to 100% of the awarded funds for direct research purposes. The Facilities cost rate budgeted is to be applied to the entire award project period.

• Indirect Costs
Indirect costs will be limited to 20 percent 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, and subcontract amounts in excess of $25,000. Applicants may use lower Indirect cost rates and use up to 100% of the awarded funds for direct research purposes. The Indirect cost rate budgeted is to be applied to the entire award project period.

See appendices D-H (for NIH, MOST/Tonji, BMBF, and InStem, respectively) for details concerning CFP allowable costs.

6. Related Business Entities (included in Part A)
All applicants (including, if applicable, a Co-PI, a Funding Partner applicant institution (e.g. Partner PI and/or a Translation Partner company) must provide information on related business entities for any application that, if awarded, would fund a for-profit organization either as: 1) the applicant organization, 2) a subcontractor or 3) the employer of a co-investigator, consultant or subcontractor. If for-profit funding is sought, include the following for each for-profit organization to be funded:

- A list of any parent organization that owns 50% or more of the for-profit's voting shares;
- A list of all subsidiaries in which the for-profit owns 50% or more of the voting shares; and
- A list of all other related business entities (i.e., entities with which the for-profit shares management and control, or shares a controlling owner).

7. Target Product Profile (up to 2 pages in Part B)
Provide a target product profile for the proposed novel development candidate/intervention. A draft guidance document from the FDA on the target product profile can be found at: www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm080593.pdf. The target product profile reflects key attributes known or required/desired for the proposed development candidate/intervention. The target product profile becomes the drug label. It therefore guides preclinical and clinical research and development and is continually refined. Briefly address each of the following components of a target product profile: a) Description of the Proposed Development Candidate/Intervention; c) Proposed Disease/Injury Indication; d) Desired Activity, in vitro/in vivo; e) Desired Safety Profile, d) Desired Dose, Route and Regimen.

8. Objective and Milestones (up to 2 pages in Part B)

State and explain the objective of the research proposed in the application. List and describe two to six major milestones of the research to establish the key requirements to achieve POC (DCF award) or a development candidate (DC award) within three years. Key activities required for achievement of a DC are listed in section II.A and Appendix A. Milestones are critical, quantifiable, and reliable indicators of the project's progress, not simply research to be performed. Indicate the time when each milestone is to be achieved (e.g. 2QY2) and the investigator responsible for achieving it (PI, and if applicable Co-PI, Partner PI, Translation Partner). Provide measurable quantifiable success criteria for each milestone. Examples of milestones and success criteria can be found in Appendix A.

9. Scientific Rationale, Significance and Responsiveness (up to 1 page in Part B)

Describe the scientific rationale for the target for intervention and for the proposed approach. Discuss how the proposed development candidate/intervention addresses an unmet medical need that, if successfully developed and made available to patients, will represent a significant improvement upon the current standard of care. Comment on the potential impact on disease, injury or medical practice. For DCF proposals, justify how the proposed approach could have a transformative or paradigm shifting impact upon regenerative medicine.

Address how the proposed research meets one of the following criteria:

- Human stem cells are necessary to achieve the outcomes of the proposed research.
- Direct reprogramming of human cells is necessary to achieve the outcomes of the proposed research.
- Human endogenous stem cells are convincingly targeted.
- Human cancer stem cells, as defined in section X.A.2.a, are convincingly targeted.

If the proposed development candidate/intervention is already represented in CIRM's current Translation Portfolio (see Appendix B) justify why the proposed research would be a compelling addition.

10. Preliminary Data (up to 3 pages in Part B)

Summarize the preliminary data and other supporting (e.g. published) results that support the proposed research. For approaches targeting cancer stem cells, provide convincing evidence that cancer stem cells are targeted as described above in the Review Criteria, Section X.A.2.a. Present preliminary data for successful application of the technologies and methodologies proposed. Clearly indicate data generated by the applicant PI and, if applicable, by a Co-PI, Partner PI and/or Translation Partner. Clearly distinguish technologies/methodologies used by the applicant PI and, if applicable, by a Co-PI, Partner PI and/or Translation Partner.

11. Research Plan (up to 5 pages in Part B)
Describe concisely, but with sufficient detail, the research plan for achieving the project objective and milestones within three years. For proposals including Co-PIs, Partner PIs and/or Translation Partners, clearly indicate proposed activities to be conducted by the applicant PI, Co-PI and/or Partner PI, and/or Translation Partner. Describe the experimental approaches, methods and techniques proposed to achieve the research objective and milestones. Identify novel or risky aspects of the research, anticipated pitfalls, and describe alternative approaches should the initial approaches fail. Address all activities required to achieve the program objective; see Appendix A for representative activities for each type of therapeutic. Assuming success, describe plans for funding and moving the project forward into IND-enabling preclinical and clinical development.

12. Timeline (up to 1 page in Part B)
Provide graphical representation of the timeline for achieving the project's objective and milestones.

13. Collaborations, Resources and Environment (up to 2 pages in Part B)
Successful collaborations are those that bring critical intellectual, technical or infrastructure resources to the project. When collaborations (intra- or inter-institutional, including collaborations with a Co-PI or with a Partner PI funded by CFP are part of the research plan, describe the nature of the collaboration and explain why it is integral to the success of the project. For applications that designate a Translation Partner, provide letters of commitment describing the partner's engagement including commitment of matching funds (above the CIRM funding) and/or resources (e.g. FTEs) that will be dedicated to the proposed project. Discuss how the PI will ensure communication, coordination and collaboration among the team members. If advisors, consultants or subcontractors will provide expertise or resources critical to the success of the project, summarize their credentials and relevant track records.

Provide a short description of the facilities, core services and environment(s) in which the research will be done, and the major equipment and resources available for conducting the proposed research. Discuss ways in which the proposed studies will benefit from unique features of the environment(s).

Provide evidence of institutional support for the PI (the Co-PI and the Partner PI, if applicable) and for translational research.

14. Assets *(up to 1 page in Part B)*
Discuss relevant assets such as intellectual property (patent applications, patents) and licenses that are available to the project. Intellectual property assets are important for proposed development candidates that must be commercialized to bring benefit to patients. For programs with Translation Partners, describe the

partner's rights to option or license inventions or data generated under the award, if available. When proprietary cell lines, small molecules, antibodies or other critical materials that are not readily available are required for the project (e.g. are the potential/proposed development candidate), provide appropriate material transfer agreements (MTAs) for their use. If MTAs are not available, provide appropriate letters of commitment from the asset owner.

15. References (up to 2 pages in Part B)
List all references used in the body of the proposal.

D. Full Application Submission Instructions

Full Applications will only be accepted from applicants who 1) submitted a PreApp and 2) are invited by CIRM to submit a full Application.

All five parts of the Early Translational IV application must be submitted together and received by CIRM no later than 5:00PM PDT on March 20, 2013 in electronic form via the Grants Management Portal (https://grants.cirm.ca.gov). It is the applicant's responsibility to meet this deadline; no exceptions will be made.

E. Submission of Supplemental Information

If necessary, the PI may submit limited supplemental materials that provide critical new information related to their research proposal after the application deadline but not later than 5:00pm PDT on May 1, 2013. Supplementary materials will not be accepted after this deadline. CIRM will accept a one-time-only submission of materials from the PI only if it meets the submission deadline and conforms to the requirements described herein. Accepted submissions will be forwarded to reviewers for their consideration.

The submission should be in the form of a one-page letter addressed to the Senior Review Officer and submitted via email to gsambrano@cirm.ca.gov. The body of the letter may not exceed 500 words and should briefly describe the type of information submitted and when the information became available. The following materials qualify for submissions of supplemental materials.

Within the one page letter provide:

1. Specific citation(s) to journal publications related to the proposed project that were published or accepted for publication since the application submission deadline. You may briefly describe the significance of the publication(s) to the proposal in the cover letter.

2. Confirmation of funding secured from other sources or regulatory (e.g., IND, IDE) filings or approvals acquired since the application submission deadline.

3. Notice of patent application(s) filed, notice of allowance received or patent(s) issued, or notice of license(s) to relevant intellectual property (granted or received) since the application submission deadline.

The letter may not be used to describe any additional data or experiments. Changes in scope, experimental approach, or research design are not allowed.

XIII. Schedule of Deadlines and Reviews

Pre-Applications due	5:00 pm (PDT), October 26, 2012
Invitations for full Applications sent out by CIRM	Late January, 2013
Full Applications due	5:00 pm (PDT), March 20, 2013
Review of full Applications by Grants Working Group (GWG)	June, 2013
Review and Approval by ICOC	Summer 2013
Earliest Funding of Awards	Fall 2013

XIV. Contacts

For information about this RFA or the review process:

Gilberto R. Sambrano, Ph.D.
Senior Review Officer
California Institute for Regenerative Medicine
Email: gsambrano@cirm.ca.gov
Phone: (415) 396-9103

XV. 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.