CALIFORNIA'S STEM CELL AGENCY

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

RFA 14-03: CIRM Strategic Partnership IV Awards

I. Purpose

The purpose of the Strategic Partnership Awards Initiative ("Initiative") is to attract industry engagement and investment in CIRM funded stem cell research. The intent of the Initiative is to create incentives and processes that will: (i) enhance the likelihood that CIRM funded projects will obtain funding for future clinical trials (e.g. follow-on financing), (ii) provide a source of co-funding for the earlier stages of clinical development, and (iii) enable CIRM funded projects to access expertise within pharmaceutical and large biotechnology partners in areas such as discovery, preclinical, regulatory, clinical trial design and manufacturing process development.

This Initiative requires applicants to show evidence of either having the financial capacity to move the project through development or of being able to attract the capital to do so. This may be evidenced by, for example, (i) significant investment by venture capital firms, large biotechnology or pharmaceutical companies, disease foundations and/or through the public markets; and financial statements evidencing significant liquid assets; or (ii) a collaborative research agreement with a large biotechnology or pharmaceutical company executed at least two weeks prior to the review by the Application Review subcommittee of CIRM's Governing Board, the Independent Citizen's Oversight Committee (the "ICOC"); such review will be approximately Q1, 2015. These requirements are described further in Section V.D. The agreement with the large biotechnology or pharmaceutical company needs only cover co-funding and collaboration support for the proposed project (and not future development).

CIRM intends to offer repeat calls under this initiative every 6-9 months. The focus, scope and objective may differ with each solicitation.

RFA 14-03: AWARDS

II. Objectives and Scope

A. Objective

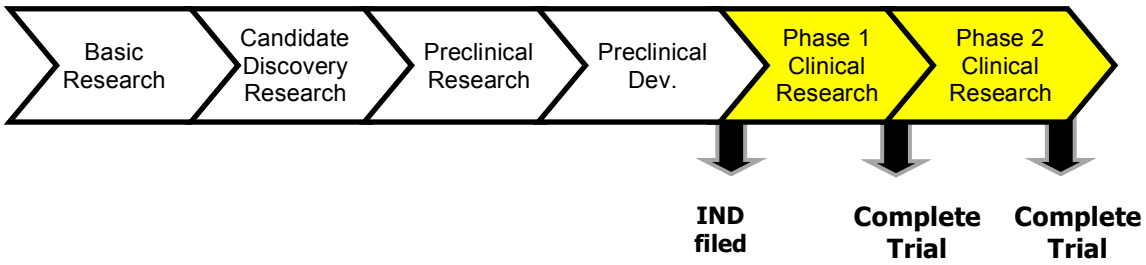
The objective of a Strategic Partnership IV award will be to complete a Phase 1 or Phase 2 clinical trial within 3 years. Proposed projects will complete one of the following:

- A Phase 1 clinical study to demonstrate preliminary safety, assess measures of biological/clinical activity in humans, and determine a range of safe doses to be studied in subsequent trials.
- A Phase 2 clinical study to evaluate both safety and efficacy of the candidate therapy.

CIRM's Strategic Partnership IV is focused on mature clinical stage projects. CIRM will only fund programs for which a complete Investigational New Drug (IND) package has been filed with the Food and Drug Administration (FDA) by no later than September 9, 2014 (Application due date). For RFA 14-03, a clinical trial will be considered "complete" upon completion of enrollment, database lock and initial assessment of outcomes of the primary and secondary study objectives.

B. Scope

The scope of the Strategic Partnership IV Awards (RFA 14-03) is illustrated in the figure below.



The key objective of a Strategic Partnership IV award is to complete a clinical trial. An RFA14-03 award will support activities that meet this objective, including, but not limited to, the activities listed below:

- All activities necessary to initiate and complete an early clinical trial (Phase 1 or Phase 2) for a single therapeutic candidate, under a single IND.

- Supporting activities to enable the proposed clinical study such as cGMP production and/or further qualification/validation of relevant assays.

- Supporting studies performed in the context of the proposed trial that will provide critical additional data to better inform decisions on continued clinical testing. Applicants will be expected to justify how such studies will specifically inform the trial results and contribute to decision making.

- Process development activities necessary to enable further development of the therapeutic candidate such as optimization of cGMP production or development and validation of a potency assay.

In general, CIRM funding must be used to support research in California (see Section VIII.B.5 for a more detailed discussion of allowable uses of CIRM funding).

Research activities that fall outside the scope of this RFA include the following examples:

- Preclinical development activities up to and including IND filing

- More than one clinical trial

- Phase 3 clinical studies

- Early research and translation activities leading up to selection of a therapeutic development candidate

- cGMP production for Phase 3 studies

- Preclinical activities to enable removal of a clinical hold

- Non-interventional clinical studies (e.g. biomarker discovery; clinical studies not involving administration of the proposed therapy; or studies using samples not from subjects of the proposed clinical studies)

- Development and qualification of a medical device for the delivery of a product other than the product proposed in the funded project

C. Priority Areas

Priority for the funding allotted for Strategic Partnership IV will be given to eligible proposals that meet one or more of CIRM's priorities for RFA 14-03, listed below:

- Proposals aimed at furthering the development of successfully completed CIRM-funded projects.
- Proposals from applicants that have secured a research development agreement with a large biotechnology or pharmaceutical company committed to providing financial support for the proposed candidate.
- Proposals that cannot, or are unlikely to, receive timely or sufficient federal funding.

III. Award Information

A. Award

Under RFA 14-03, CIRM intends to commit up to $32M to support up to 3 development projects. CIRM will fund up to $10M of the total costs of a proposed project over three years or less (justifiable costs include direct project costs, facilities costs, and indirect costs). In *exceptional circumstances*, there is the potential to increase the award up to $12M per application, only if fully justified, recommended by the GWG, and approved by the Application Review Subcommittee of the ICOC. For all proposals, co-funding is required (see Section III.B). The application must include a fully justified, detailed, activity-based budget, which identifies activities that CIRM will fund; those that the applicant will fund and as relevant, those activities its biopharmaceutical partner, will fund.

B. Co-Funding

Under a RFA14-03 award, CIRM will require co-funding from the applicant, which may come from the applicant's own assets, from an industry partner, or from another funding source arranged by the applicant. Applicants must match at least 100% of the total CIRM funding requested (i.e. at least a 1 to 1 match). In their application, applicants will be required to address the status and sources of co-funding required for achievement of the RFA objective. The biopharmaceutical partner's co-funding may be provided in the form of capital or justifiable in-kind services.

C. Budgets, Milestones and CIRM Oversight

For all RFA14-03 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). In addition, CIRM will work with the PI to ensure that the team includes the necessary project management expertise, and reserves the right to approve the selection of a project manager. Progress in translational research is important to CIRM. Continued funding is contingent upon timely progress, as outlined in the project milestones and timeline established under the NGA or NLA, and the on-going ability of the applicant to fund its operations and to satisfy its co-funding commitment; continued funding decisions will also take into consideration competitiveness of the candidate therapy and the feasibility of subsequent development. CIRM reserves the right to terminate the project or to negotiate new milestones to refocus/redirect the project if agreed to milestones are not achieved, or if there are significant changes in the competitive landscape or feasibility of the development program.

The Grants Administration Policy (GAP; see Section XI.A) requires that the grant or loan recipient submit annual Progress Reports to CIRM and provide notification of any serious adverse event related to the therapeutic candidate in a clinical trial. In addition, communication and reporting responsibilities of the grant or loan recipient to CIRM will include: 1) quarterly updates; 2) routine communication by the Principal Investigator (PI) or Project Manager; 3) discussion with CIRM's Clinical Development Advisory Panel (CDAP) approximately annually and/or at key decision points, 4) receipt of key regulatory documentation such as the pre-IND briefing package, formal minutes from agency meetings or other key agency correspondence and 5) participation of CIRM representatives as observers in key regulatory meetings.

D. Covered Clinical Trial Costs

CIRM requires that clinical trials proposed for funding must include clinical trial sites in California. If the total number of clinical sites proposed for the clinical study is less than 20, at least one clinical site must be in California. For trials proposing 20 or more clinical sites, at least 10% of the sites must be in California.

Only applicants that have demonstrated a sufficient presence in California (as described in Section V.C) are eligible for funding. Covered costs may include costs of clinical trials conducted outside of California as part of the funded project; see Section VIII.B.5 for further explanation of permissible expenses. CIRM expects funded clinical trials to include women and members of minority groups unless a clear and compelling rationale and justification establishes to the satisfaction of CIRM, that such inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.

E. Contracts

CIRM has the option to review (for compliance with CIRM's policies and regulations and the advancement of its mission) contract/agreements (e.g. including, but not limited to, those with Contract Research Organizations (CROs) or Contract Manufacturing Organizations (CMOs) which it deems critical to the success of the project. Upon request, the awardee will be required to provide such documentation.

F. Commencement/Other CIRM Awards

Given the urgency of CIRM's mission, all approved applications must be initiated (award start date in issued and signed NGA or NLA) within 6 months of approval and authorization for funding by the Application Review Subcommittee of the ICOC, unless CIRM's President grants an extension based upon compelling justification of the need for additional time. In the case of awards to applicants that already have a CIRM award such as a Disease Team I award, any funding disbursed to the applicant under this RFA must be for activities not funded by the already existing award.

IV. Award Mechanism

CIRM expects to fund approved proposals through grants or loans. RFA 14-03 awards to non-profit organizations will be in the form of a grant. For-profit applicants may choose to accept the award in the form of a grant or a loan.

Grants under this RFA are funded through quarterly or semi-annual disbursements (at CIRM's option) and are subject to the revenue sharing provisions in CIRM's regulations (Intellectual Property and Revenue Sharing Requirements for Non-Profit and For-Profit Grantees (17 Cal. Code Regs. § 100600 et seq.).

Loan recipients shall be governed by the CIRM Loan Administration Policy (LAP) that is in effect as of the date of the execution of the NLA. Approved applicants who accept a loan will pay for loan administration costs and the costs of CIRM's due diligence review out of funds included in the award. Loan applicants will be required to submit financial information in connection with CIRM's due diligence.

The terms of the Loan are set forth in detail in Appendix A. For additional information on the loan program, consult the CIRM LAP, available here.

V. Eligibility

For an **investigator-sponsored IND**, the investigator-sponsor must be the PI on the CIRM application.

For an **organization-sponsored IND**, the organization sponsor must be the applicant organization on the CIRM application, and the PI must be an employee of the applicant organization.

A. Project Eligibility

1. Project Objective: The proposed project must address a serious unmet medical need/injury and must include the completion, in 3 years or less, of a Phase 1 or Phase 2 clinical trial for a single therapeutic candidate, under a single Investigational New Drug (IND) application filed with the Food and Drug Administration (FDA). The proposed clinical trial will evaluate preliminary safety and assess measures of preliminary biological activity/efficacy in humans.

2. Therapeutic Candidate: Each proposed project must be focused on a single therapeutic candidate (that is, or will be, the subject of a single IND filing) that meets any of the following criteria:

   - A cell therapy derived from pluripotent stem cells
   - Allogeneic tissue-derived stem cells or progenitor cells for repair/regeneration
   - Stem cell-engineered functional tissues for implantation in vivo
   - A small molecule or biologic demonstrated to target normal endogenous stem cells in vivo as the primary mechanism of action (MOA) for repair/regeneration
   - Genetically or pharmacologically-modified hematopoietic or other tissue stem cells (includes autologous or allogeneic approaches)

Therapeutic candidates that fall outside the scope of this RFA include the following:

- Unmodified hematopoietic stem cells (HSCs)
- Small molecules and biologics, unless specifically targeting endogenous stem cells for repair/regeneration as the primary MOA
- Autologous mesenchymal stem cell (MSC) approaches
- Autologous tissue-derived stem cell approaches
- Minimally manipulated bone-marrow or minimally manipulated cord-blood

3. Readiness: The Strategic Partnership IV RFA 14-03 is designed to capture mature clinical stage projects for which a complete Investigational New Drug (IND) package has been filed with the Food and Drug Administration (FDA) no later than September 9, 2014 (Application due date).

Eligible projects for RFA 14-03 will meet the following criteria:

- A single final therapeutic development candidate has been chosen, for which there is strong scientific and clinical rationale.
- Strong preclinical proof-of-concept (POC) evidence exists to support use of the candidate in the target disease/injury (for example, reproducible evidence of disease modifying activity in a relevant animal model using the intended therapeutic candidate).
- Applicants must have submitted an IND package to the FDA no later than September 9, 2014 (Application due date). Applicants whose IND is placed on clinical hold by the FDA must inform CIRM and provide both the FDA comments and plan for resolving the clinical hold issues no later than December 01, 2014. All clinical hold issues should be projected to be resolved by the time of funding.
- For projects ready to start a Phase 2 clinical trial, applicants must have Phase 1 data demonstrating preliminary safety in the target population, by the application due date (September 9, 2014).

4. Commercial Validation: In addition, applicants must provide Evidence of Commercial Validation (Section V.D).

B. Institutional Eligibility

Applicant organizations must demonstrate a sufficient presence in California (as described in Section V.C) to be eligible for funding. All applicants must also provide evidence of commercial validation to be eligible for this award (Section V.D). Both non-profit and for-profit organizations may apply for an award under RFA 14-03.

“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 are also referred to as “commercial organizations”.

A for-profit applicant organization may submit only one application to RFA 14-03. For-profit applicant organizations that hold 2 or more of the following awards: Disease Team, Disease Team Therapy Development, or Strategic Partnership, as of the application due date, September 9, 2014, are not eligible to apply for this award.

C. California Presence

By the Application Date (September 9, 2014): If the applicant organization does not already have operations located in California, it must describe the plan to establish operations in California from which the project will be performed. CIRM will require evidence that operations are in place in California prior to the start of CIRM funding.

To receive CIRM funding, the applicant must show the following ties to California:

1. To qualify for any CIRM funding, an applicant organization must have at least 2 full-time equivalent (FTE) identified as key personnel on the application, in California during the project period who are working on the CIRM funded Project. In addition to the 2 full-time equivalent key personnel, the PI is expected to spend at least 30% time in California, working on the approved project.

2. In addition to the minimum requirement of 2 FTEs and a PI with at least 30% effort in California, as described in Section V.C.1, for an applicant organizations having more than 30 employees world-wide, the applicant organization may use CIRM funds for clinical trials sites located outside California but within the United States if:

   (i) Within 6 months of the start of the CIRM-funded project, such applicant organizations have the lesser of (a) an additional 5% or greater of their workforce located in California, or (b) 50 or more employees in California.

   (ii) For an applicant organization that does not satisfy the requirements of subparagraph (i), above, the organization may not use CIRM funds for clinical trial sites that are outside of California.

These conditions only apply to the use of CIRM funds. An organization may use its Co-Funding budget to support clinical trial sites that are outside California.

D. Evidence of Commercial Validation

In order to attract projects having or likely to attract industry investment, including follow-on financing of Phase 3 clinical trials, or having adequate self-funding, applicants must provide evidence of commercial validation as part of the Letter of Intent (LOI) submission. Such evidence will require submission of supporting documentation, satisfying at least one of the following:

1. Financial Strength and Historical Investment:
   The applicant is a for-profit that has (a) obtained in the past two years, an equity and/or programmatic investment through the public markets or by venture capital firms, biotechnology or pharmaceutical companies, non-profit foundations or government entities, in the amount of at least $10M **AND** (b) at least one year of balance sheet cash or cash equivalents (as demonstrated by its most recent financial statements and pro-forma for any concurrent investment) based on the last twelve months (LTM) operating cash burn rate, without taking into account any funds provided by CIRM, but including the first 12 months of co-funding to be provided by the applicant if awarded the CIRM grant or loan. For purposes of RFA 14-03, LTM operating cash burn is defined as cash flow from operations, less capital expenditures and any debt service.

   AND/OR

2. Agreement with a Biopharmaceutical Partner:
   If the applicant is a non-profit or a for-profit that is seeking to establish commercial validation by virtue of a collaborative research agreement with a large biotechnology or pharmaceutical company that has a market capitalization of at least $500M and that agrees to provide the financial and/or in-kind support for the at least 1:1 match required by RFA 14-03, the applicant should submit a fully executed copy of such agreement if one already exists. If such an agreement has not yet been entered into, by the due date of the LOI (June 19, 2014) the applicant must provide a letter from the biotechnology or pharmaceutical company indicating its interest in co-funding the proposed project and that the parties are negotiating the terms of support. The applicant must submit a term sheet and/or letter of intent outlining terms of the company's funding support, signed by the company, by the date that Supplemental Information must be filed (November 15, 2014) and a fully executed agreement must be provided by two weeks prior to the date of the ICOC/Application Review Subcommittee meeting to approve and authorize funding for Strategic Partnership IV awards (Q1, 2015; exact date to be determined).

See Section VIII.A for specifics of documentation required as part of the LOI and Application. **The agreement with the biotechnology or pharmaceutical company** needs only cover co-funding and collaboration support for the proposed project (and not future development). To that end, the agreement can be in the form of an option, license, funded research collaboration or sponsored research agreement or similar agreement, as long as it provides for a level of co-funding and/or in-kind services sufficient to permit the applicant to meet its co-funding obligations.

If CIRM determines that these requirements are not met, it may terminate all further action on the application.

E. Principal Investigator (PI) Eligibility

CIRM requires that a single PI and a single applicant organization (the PI's organization) be designated in a RFA 14-03 application. The PI is the designated point of contact for CIRM and is the person responsible and accountable to CIRM for scientific performance on the project. The applicant organization is the designated contact institution for all financial and other administrative considerations.

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

- Be an employee of the applicant organization who commits at least 30 percent time working on the project out of the California office of the applicant organization, and have demonstrated expertise in drug development and in managing clinical research programs.
- Have documented authority from the applicant organization to staff the proposed project in California.
- Have documented commitment from the applicant organization to provide resources sufficient to carry out the proposed research.

In order to ensure effective leadership of this development stage program, CIRM is limiting the number of active CIRM Disease Team, Disease Team Therapy Development, or Strategic Partnership awards in which an investigator may participate as a PI or a Co-PI. Unless the proposed project is a *continuation* of a previous CIRM-funded Disease Team or Disease Team Therapy Development project, RFA14-03 is not open to investigators who are already a PI or a Co-PI on an active CIRM Disease Team, Disease Team Therapy Development or Strategic Partnership award as of September 9, 2014, the deadline for submission of the full application.

In addition, 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 *overall* active CIRM research awards in which an investigator may participate as PI or Co-PI. RFA 14-03 is not open to investigators who are already a PI or Co-PI on 2 or more active CIRM awards as of September 9, 2014, 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: Shared Research Labs, Major Facilities, Research Training Awards I & II, Bridges to Stem Cell Research, or Conference Grants.

F. Project Manager Eligibility

CIRM requires a project management professional (Project Manager) be designated in each RFA 14-03 Award application. The Project Manager must have relevant experience in managing clinical development programs and must be able to devote an appropriate (≥50%) percentage effort, in California, to the project.

G. Extraordinary Exceptions

In extraordinary circumstances, the President has the discretion to permit exceptions to requirements or limitations in Sections V and VIII.A. The exercise of such discretion will be only in exceptional cases where the applicant has demonstrated that such an exemption 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 (GAP; Section XI.A) and the Loan Administration Policy (LAP; Appendix A), or they will not be considered. Exceptions may include permitting the disbursement of initial funding while an out-of-state company is in the process of building its operation in California, upon a showing of a good faith effort to adhere to the requirements above and upon terms and conditions which will be imposed pursuant to such exception.

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 must request it at least 14 days before the LOI deadline or 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 X.

VI. Application and Evaluation Processes

Submission of an application for a Strategic Partnership IV Award (RFA 14-03) involves a two-step process. An eligible applicant (see Section V for eligibility criteria) must first submit a Letter of Intent (LOI). Applicants will be notified if their LOI is **NOT** accepted.

In the second step of the process, eligible applicants will submit a full application. Applications will only be accepted from applicants that meet all eligibility requirements and have submitted an LOI that was accepted by CIRM.

A. Application Review Process

Applications for the CIRM Strategic Partnership IV Awards 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 (ICOC), and the Chair of the Governing Board. The list of scientific members who may participate in the GWG review can be found here. The composition of the ICOC can be viewed here.

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 VII. The entire GWG will make funding recommendations based on scientific merit. The Board's Application Review Subcommittee will make funding decisions based on the GWG recommendations, any staff recommendations and a programmatic review.

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 and external reviewers and members of the CDAP. (Per Gov. Code §6254.5(e) non-public records may be disclosed to government agencies under confidentiality agreements). The policies, procedures and laws that address confidentiality of records submitted to CIRM are described in Section XII.

VII. Review Criteria

Applications for RFA 14-03 will be evaluated for scientific merit by the GWG in five key areas: A. Significance and Impact; B. Scientific Rationale and Risk/Benefit; C. Design and Feasibility; D. Principal Investigator, Development Team and Leadership Plan; and E. Quality of Collaborators, Assets, Resources and Environment. The specific criteria for review of applications are based on the standard review criteria described in the CIRM GAP (Section XI.A).

The GWG will be asked to give special consideration to CIRM's priorities for this

RFA (Section II C).

A. Significance and Impact

1. Target Product Profile: Reviewers will assess how well the target product profile (TPP) proposed in the application conveys the long term aspirational product attributes and overall intent of the development program and whether it provides appropriate metrics for achievement of key attributes.

2. Clinical Competitiveness and Impact: Where a due diligence investigation has been conducted in regard to the proposed therapeutic, reviewers will assess if the investigation was thorough in evaluating the potential for a competitive product. Reviewers will evaluate whether the proposed therapeutic candidate could have a significant impact on the target disease/injury and if it would offer clinically meaningful advantages over current therapies on the market or in late stage development. Reviewers will also assess if the proposed project could advance the field of stem cell-based/regenerative medicine.

3. Responsiveness**:** Reviewers will assess the overall relevance of the project to stem cell-based and regenerative medicine and the body of evidence that the therapeutic has a strong and compelling stem cell connection. Reviewers will assess whether the proposed activities are within scope as defined in Section II and whether the proposed project should receive priority as stated in Sections II and VI.

B. Scientific Rationale and Risk/Benefit

Where a potential or existing partner has conducted a due diligence investigation on rationale and risk/benefit for the proposed therapeutic, reviewers will assess whether the investigation was thorough. Reviewers will assess if there is a strong scientific rationale and a favorable risk/benefit ratio for the proposed therapeutic intervention in the target disease/injury. Reviewers will assess if, based on the preclinical data and any available clinical data, there is a reasonable expectation that the proposed therapeutic approach will have a meaningful clinical benefit for patients and if the potential risks to subjects are manageable and acceptable in the context of the target patient population.

C. Design and Feasibility

Reviewers will assess the following**:**

1. Overall Development Plan: Applications will be assessed for the quality of the Development Plan. Under this RFA, proposed projects for a Phase 1 clinical trial are expected to include a well thought out development plan through the end of End-of-Phase 2 (defined herein as completion of clinical studies providing sufficient information on safety, efficacy and dose to enable the transition to Phase 3). Those applicants proposing a Phase 2 clinical trial are expected to include a development plan that includes the pivotal trials to gain Marketing Approval; this plan should be realizable and should support achievement of the Target Product Profile.

2. Project Plan: The Project Plan describes the scope of work that will be conducted during the award period. Reviewers will evaluate the design and feasibility of the Project Plan with respect to the following:

    - Is the proposed project integral to the Overall Development Plan?
    - Is the overall Project Plan feasible and could it meet the objective of RFA 14-03, which is to complete a clinical trial within the project period?
    - Is the clinical operations plan adequate to support successful execution and oversight of the clinical trial?
    - Do the project milestones capture key activities and are they reliable indicators of the project's progress?
    - Are the criteria for Go/No Go decisions adequately defined?
    - Is the project timeline realistic and achievable?

1. Key Project Components:

    a. Design and Feasibility of the Proposed *Clinical Study*:

    - It is expected that any clinical trial proposed for funding under RFA 14-03 will be designed to inform decisions on further development of the candidate therapy and to inform the design of subsequent clinical trials. Reviewers will assess how well this criterion is met.
    - Reviewers will assess if the proposed clinical study is well designed and is likely to achieve the RFA objectives of evaluating both preliminary safety and assessing measures of biological activity/efficacy in humans.
    - Reviewers will assess whether the choice of patient population is appropriate.
    - Reviewers will assess whether the efficacy endpoints or proposed biomarkers of activity are appropriate and provide objective measures of success and whether the study design and proposed endpoints are appropriate to inform continued development of the candidate therapy.

- Reviewers will assess whether the enrollment projections are realistic; whether the proposed study is likely to be completed during the award period and whether the appropriate mitigation strategies are in place to address delayed enrollment.
- In addition reviewers will evaluate to what extent the proposed trial design is likely to test or elucidate mechanism(s) of action of the therapeutic candidate such that, regardless of clinical outcome, information will be gained.

b. Feasibility of the *Regulatory Path*: Reviewers will assess the proposed project with respect to the following:

   If the proposed clinical study is on clinical hold, whether it is feasible to expect that all clinical hold issues will be addressed by the time of funding (i.e. within 6 months of approval for funding by the ICOC/Application Review Subcommittee in Q1, 2015).

c. Feasibility of the *Manufacturing Strategy*: Reviewers will assess to what extent and how well the following questions have been addressed in the proposed project:

   - Is the manufacturing strategy feasible to supply the proposed clinical trial and are mitigation strategies appropriate to address manufacturing bottlenecks?
   - Will the manufacturing process support scale up for future larger trials and commercialization?
   - Are there steps in the manufacturing process that could adversely impact clinical adoption?
   - If a medical device will be used to deliver the intended therapeutic candidate to the patients, is the medical device approved by the FDA for the proposed clinical indication?

D. Principal Investigator (PI), Development Team and Leadership Plan

Reviewers will assess to what extent and how well the proposed project meets the following criteria with respect to the qualifications of the development team:

1. Expertise and Track Record of PI: Does the PI has relevant experience in therapy development and demonstrated successful leadership experience?

2. Expertise and Track Record of Project Manager: Does the Project Manager has relevant expertise and demonstrated project management experience in clinical development studies?

3. Development Team and Leadership Plan: Has an appropriate multidisciplinary team been assembled to execute the project? Does the team include a Product Development Lead, CMC Lead, Clinical Lead, and a Regulatory Lead in addition to the required Project Manager? Do these team leads have demonstrated expertise in their functional area? Has the PI developed a leadership and communication plan that will ensure successful execution of the project? Does the plan include methods for progress monitoring, project decision-making and conflict resolution?

4. Clinical Investigators at Clinical Sites: Do the lead clinical investigators have relevant experience in the target disease area and in conducting clinical studies?

5. Budget: Reviewers will assess whether the activities proposed and budget allocated are reasonable to allow completion of the project during the award period (3 years)?

E. Collaborations, Assets, Resources and Environment

Reviewers will assess the proposed project with respect to the following:

1. Collaborations: Are collaborations in place (including those with a co-funding partner) that will be needed for the success of the project?

2. Clinical Sites: Are the proposed clinical sites experienced in conducting Phase 1 and Phase 2 trials? Are the proposed clinical sites sufficiently likely to enroll patients for completion of the trial within the 3-year project period?

3. Assets: Reviewers will be asked to note if the critical assets (e.g. patent applications, patents, Material Transfer Agreements, or license agreements, Drug, Device or Facility Master File(s)) that are necessary to enable development of the therapeutic candidate are either absent in the proposal or not at an adequate stage of negotiation to enable and justify investment in the development and future clinical testing and commercialization of the proposed product (see section VIII.B, Part J and Part I). CIRM will evaluate the status of critical assets prior to funding.

4. Contract Services: Do the proposed CROs/CMOs/consultants have the experience and expertise necessary to successfully meet expectations, deliverables and timelines? Does the development team have appropriate oversight expertise?

5. Resources and Environment: Are the necessary facilities, major equipment, and services available for conducting the proposed research?

VIII. Application Procedure

Applicants must follow these instructions for submission of a Letter of Intent (LOI) and a Strategic Partnership IV award application (RFA 14-03). Applicants will be notified if their LOI was **NOT** accepted.

Applications will only be accepted from PIs who submitted a LOI that was accepted by CIRM. The PI and the project proposed in the application must be the same as those described in the LOI; otherwise, the application is deemed ineligible.

A. Letter of Intent (LOI) and Commercial Validation

A PI may submit only a single LOI for this RFA using the forms and instructions provided in the Grants Management Portal here. The LOI should concisely describe the proposed project and explain how it will, within three years, achieve the objective of the RFA14-03, which is to complete a Phase 1 or Phase 2 clinical trial. Documentation in support of commercial validation is required as part of the LOI submission. See below and refer to the LOI instructions and form.

Commercial Validation

Evidence of Commercial Validation must be provided as part of the LOI submission and consists of the following.

1. **If the applicant organization is a for-profit** and is seeking to establish commercial validation through demonstration of financial strength and historical investment (see Section V.D.1), provide documentation showing that the applicant has:

   (a) Obtained in the past two years, an equity and/or programmatic investment through the public markets or by venture capital firms, biotechnology or pharmaceutical companies, non-profit foundations or government entities in the amount of at least $10M **AND**
   (b) At least one year of balance sheet cash or cash equivalents (as demonstrated by its most recent financial statements and pro-forma for any concurrent investment) based on the last twelve months (LTM) operating cash burn rate, without taking into account any funds provided by CIRM, but including the first 12 months of the applicant's co-funding obligation **AND**
   (c) For purposes of RFA 14-03, LTM operating cash burn is defined as cash flow from operations, less capital expenditures and any debt service.

Specific documents that should be provided are:

- Financial statements prepared in accordance with US GAAP for the quarters ended March 31, 2013 and March 31, 2014, as well as year ended December 31, 2013.
- Documents sufficient to establish the amount invested by venture capital firms, large biotechnology or pharmaceutical companies and/or non-profit foundations, including supporting data such as a capitalization table, to demonstrate $10M in prior investment. When available, (even if subsequent to the LOI deadline), applicant will provide financial statements prepared in accordance with US GAAP for the year ended December 31, 2014.

AND/OR

2. **If the applicant is a non-profit or a for-profit** and is seeking to establish commercial validation by virtue of an agreement with a biotechnology or pharmaceutical company that has a market capitalization of at least $500 M (see Section V.D.2) and that agrees to provide the financial and/or in-kind support for the at least 1:1 match required by RFA 14-03, the applicant should submit a fully executed copy of such agreement if one already exists. If such an agreement has not yet been entered into, by the date of the LOI due under this RFA (June 19, 2014) the applicant must provide a letter from the biotechnology or pharmaceutical company indicating its interest in co-funding the proposed project and that the parties are negotiating the terms of support. The applicant must submit a term sheet and/or letter of intent relating to such agreement, signed by the partner, by the date that Supplemental Information must be filed (November 15, 2014) and a fully executed agreement must be provided by two weeks prior to the date of the ICOC/Application Review Subcommittee meeting to approve and authorize funding for Strategic Partnership IV awards (Q1, 2015).

   A term sheet or letter of intent relating to the agreement should address the following:

   - Levels of co-funding for the proposed project (need not include future development) which the applicant, with its biopharmaceutical partner, agrees to commit to the project on an annual basis and the amount it is requesting CIRM to fund annually.
   - A general description of the agreement structure with the biotechnology or industry partner (e.g. option agreement, licensing agreement with rights of termination, opt-ins, or opt-outs, etc.).
   - All payments the applicant would receive including upfront payments, any research and development support, FTE support, and milestone payments.

- The amount, nature and value of in-kind services, including but not limited to FTEs, that an industry partner will provide without charge, such as experience in regulatory affairs, process development or clinical development.

The completed LOI and supporting evidence of commercial validation must be submitted online using the CIRM Grants Management Portal here and must be received by CIRM no later than 5:00 PM (PDT) on June 19, 2014. No exceptions will be made.

B. Application Forms

A PI may submit only a single application for RFA 14-03, corresponding to the accepted LOI, using the forms and instructions provided in the Grants Management Portal here. Application forms for this RFA will be available in July, 2014.

The application for 14-03 consists of up to **ten parts**:

Part A: Application Information Form (Web-based form). Includes Abstract, Public Abstract, Statement of Benefit to California, Key Personnel, Budget, Budget Justification and Related Business Entities Disclosure (additional details in sections number 1- 6, below).

Part B: Strategic Partnership IV Award Proposal (MS Word template). Includes Target Product Profile; Clinical Competitiveness and Impact; Scientific Rationale and Risk/Benefit, Overall Clinical Development Plan to gain Marketing Approval; Project Plan with Milestones and Timeline; IND Status; Clinical Protocol Synopsis; Manufacturing Plan Synopsis; PI, Development Team and Leadership Plan; Collaborations, Assets, Resources and Environment; Clinical Sites; Clinical Operations Plan; Intellectual Property, Licenses and Agreements; References (additional details in sections number 7-20, below).

Part C: Biographical Sketches for Key Personnel (MS Word template). Includes key clinical investigators and letters of collaboration and/or institutional support.

Part D: Due Diligence Report. For projects that have undergone a due diligence analysis by a pharmaceutical/biotechnology partner resulting in an executed agreement or a term sheet or letter of intent to enter into an agreement, provide a summary and/or checklist of the due diligence investigation (additional details in section number 20, below).

Part E: Activity Based Budget

Part F: FDA Correspondence. Provide copies of all regulatory correspondence with the FDA relating to the IND submission, the proposed clinical trial, and any clinical hold issues.

Part G: Clinical Protocol. Copy of the final clinical protocol and summary of amendments must be provided

Part H: Investigator Brochure

Part I: Copies of Authorization for Cross Reference of Drug, Device or Facility Master Files

Part J: Licenses and agreements (MTAs). If you have licenses or MTAs in place, submit copies.

The Application includes the following sections:

1. Abstract *(divided in four parts of up to 3000 characters each; in Part A)*

Part 1. Project Description: Briefly describe the proposed therapeutic candidate and summarize the scientific rationale for the proposed intervention in the target disease/injury.

Part 2. Clinical Competitiveness and Impact: Describe the unmet medical need that the proposed therapy will address and explain how the proposed therapy could improve patient care compared to other therapies either available or in development.

Part 3. Proposal Overview: Summarize the proposed project plan and describe how it will (a) achieve the overall objectives of the Strategic Partnership Program, which is to leverage CIRM funding and the potential to provide follow-on funding to bring therapies through development and (b) achieve the specific objective of RFA 14-03, which is to complete a clinical study within the 3 year project period.

Part 4. Milestones: Summarize high-level milestones to be achieved within the 3−year award period.

2. Public Abstract *(up to 3000 characters; in Part A)*
In lay language, briefly describe the proposed project and explain how the proposed stem cell-derived therapy will advance the treatment of disease or serious injury in humans. This Public Abstract will become public information and will be available online; do not include proprietary or confidential information, or information that could identify the applicant and applicant organization or, if applicable, the biopharmaceutical partner.

3. Statement of Benefit to California *(up to 3000 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 and/or biopharmaceutical partner (e.g., PI name, applicant institution name or location).

4. Key Personnel *(included in Parts A and C)*
List all key personnel and their roles on the project in the relevant sections of Part A. Key personnel are defined as individuals who contribute to the scientific development or execution of the project in a substantive way, whether or not they receive salaries or compensation under the grant. Key personnel may include any staff, collaborators, or consultants who meet this definition. Key personnel who are not part of the applicant organization should be listed in the subcontract section of the application. For example, list the key lead investigator for each clinical site even though he/she will be compensated as part of a subcontract. It is not necessary to name other clinical site personnel who will be participating in the conduct of the study.
Personnel that are not key, such as technical support staff, may be supported by award funds but not named. A minimum of one percent effort is required for each key person with the exception of the PI, who is required to commit a minimum of thirty percent (30%) effort, and the Project Manager, who is required to commit a minimum of fifty percent (50%) effort.

For each key person listed, provide a two-page biographical sketch using the template provided under Part C. The biographical sketch should highlight relevant experience, in particular, team leadership, conduct of clinical studies and/or contribution to regulatory filings for product development. Include relevant publications, patents or patent applications. Following the biosketch for the PI, provide biosketches for functional area heads and/or members of the development core team (including the individuals responsible for overseeing clinical, clinical operations, regulatory, CMC, data management and translational research activities) and for the lead clinical investigator at each proposed site. Thereafter, include all remaining biosketches in alphabetical order.

5. Budget *(included in Parts A and E)*
Provide all budget information requested in the budget section of Part A and in Part E. Specify and provide well-justified budgets for subcontracts and consultants in the appropriate section in Part A. In the activities-based budget spreadsheet (Part E), detail key activities and associated costs. Include costs proposed to be funded by CIRM through this award, funded through another CIRM award, or through co-funding either by self-funding or through third parties. Proposed budgets should align with the sequence of when the activities will be conducted and must be well justified in the appropriate section of Part A. All allowable costs for research funded by CIRM are detailed in the CIRM GAP (Section XI.A).

Under RFA 14-03, CIRM-funded allowable costs include the following:

- ***Salaries for Key Personnel and other Support Staff***
  Salaries for personnel may include the PI and key technical or other 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. Exclusively allowed Indirect Costs should cover all other administrative support salaries.

- ***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 a CIRM Strategic Partnership IV Award are strongly encouraged to attend a CIRM-organized grantee meeting in California and will be required to attend Clinical Development Advisory Panel (CDAP) meetings in San Francisco at key milestones/decision points. Applicants should budget for one such meeting per year. Travel costs for these meetings should be included in the budget. Travel costs associated with collaborations necessary to the grant are allowable. Details of allowable travel costs can be found in the CIRM GAP (Section XI.A).

- ***Equipment***
  Major equipment (more than $5,000 per item) necessary for conducting the proposed research at the applicant institution should be itemized and justified. 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. Examples of such research include study design; clinical protocol development; design of a toxicology study; analysis and interpretation of data; development of new methods.

  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.)

Except as set forth in Section V.B, 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 execution of a clinical trial according to a protocol, execution of a toxicology study performed according to an existing protocol and cGMP manufacturing. (Clinical trial execution would include blinding, randomization, patient recruitment, patient treatment, medical monitoring, data collection, clinical site selection/site initiation and Institutional Review Board (IRB) activities.)

CIRM requires that clinical trials proposed for funding must include clinical trial sites in California. If the total number of clinical sites proposed for the clinical study is less than 20, at least one clinical site must be in California. For trials proposing 20 or more clinical sites, at least 10% of the sites must be in California.

- ***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 are limited to 10% for for-profit applicants, and to 15% for not-for-profit applicants, 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.

6. Related Business Entities *(included in Part A)*
In order to comply with the Conflict of Interest policies under which CIRM operates, all applicants 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 consultant or subcontractor. If the application does not seek funding for any such for-profit organizations, indicate that in this section of the form. If for-profit funding is sought, include the following for each such 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; use TPP template in Part B; also included as Sample B)*
Provide a target product profile (TPP) for the proposed therapeutic candidate. The TPP provides the aspirational attributes of the product to help define success and inform the proposed label. The TPP should articulate the overall intent of the therapeutic development program, and the studies proposed within this research proposal should be designed to collect data that will support the TPP. The TPP should provide the optimal profile (ideal) and the threshold profile (minimally acceptable to differentiate from current and future competing products), and identify criteria (metrics) for key decisions in the development process. It is a comprehensive outline of product specifications with respect to safety, effectiveness, quality, clinical evaluation, non-clinical evaluation, regulatory requirements and commercial factors e.g., market advantage and target differentiation. The TPP is a dynamic document that should be continually refined as data evolves and will ultimately become the product label.

Using the CIRM TPP template in Part B of the application (see Sample B for the template), provide the desired attributes/claims of the therapeutic for the following: indication, target activity, patient profile, efficacy endpoints, safety/contraindications, dose/regimen, dosage form and route of delivery. The FDA released the draft guidance document "Guidance for Industry and Review Staff: Target Product Profile – A Strategic Development Process Tool" which may be a helpful resource for developing a TPP. It is available from the FDA's website. It is worth noting that while this document was developed and issued by the FDA's Center for Drug Evaluation and Research, it contains many guiding principles that apply to developing a TPP for cell therapies and biological products, as well as to products regulated by the Center for Drug Evaluation and Research (CDER).

8. Clinical Competitiveness and Impact *(up to 3 pages; in Part B)*
Summarize the current standard of care and competitive landscape for the target disease/injury. Describe how the proposed novel therapy could lead to a significant improvement in patient care compared to existing therapies or to other therapies currently in late-stage development. Describe the pharmacoeconomic rationale for the proposed therapeutic. Explain how the proposed project will advance the field of stem cell-based or regenerative medicine.

9. Scientific Rationale and Risk/Benefit *(up to 10 pages; in Part B)*
Describe the scientific rationale for the proposed therapeutic intervention. Summarize the evidence supporting use of the proposed therapeutic in the target disease and provide key data. Provide a summary (in tabular form) of the key clinical trial supporting safety and efficacy studies (preclinical and clinical) and summarize major outcomes and findings (you may reference appropriate sections of the Investigator Brochure).

Describe the overall relevance of the project to stem cell-based and regenerative medicine. Summarize body of evidence that the therapeutic has a strong and compelling stem cell connection and provide key data.

Describe the potential benefits and risks of the proposed therapy and explain why the potential benefits outweigh the risks and justify use of the proposed therapeutic intervention in the target disease/injury. The Risk/Benefit analysis is based on the target patient population, other therapeutic options for that population, the scientific rationale, preclinical pharmacology and toxicology studies, and the therapeutic approach.

10. Overall Development Plan *(up to 3 pages; in Part B)*
Summarize the overall development plan. Those applicants proposing to complete a Phase 1 clinical trial should provide a well thought out development plan thru the End-of-Phase 2 (defined herein as completion of clinical studies providing sufficient information on safety, efficacy and dose to enable the transition to Phase 3). Those applicants proposing a Phase 2 clinical trial should include a development plan for a pivotal trial to gain Marketing Approval for the proposed therapeutic candidate. All applicants should provide a high-level timeline highlighting key, clinical, CMC, regulatory and other milestones and major decision points, as well as estimated costs to achieve these major milestones.

11. Project Plan, Milestones, and Timeline *(up to 8 pages plus 1 page for timeline, the latter in Gantt chart format or equivalent; in Part B)*

- ***Project Plan*****:** Describe the project plan and scope of activities proposed for funding under this award. Indicate activities to be conducted by the applicant and/or, if applicable, by the partner. Explain how the Project Plan contributes to, and advances, the overall Development Plan. Include a description of the Clinical Operation Plan using the template provided. A copy of this template has been provided as Sample E. Identify potential risks to the project and describes the mitigation strategies.

- ***Milestones***: Using the Milestone template provided in Part B of the application; list the major project milestones by project year. Indicate Progress Milestones versus Go/No Go Milestones and include target completion dates and success criteria (an example of a completed milestone template is provided in Sample A). Milestones should describe precise, quantifiable outcomes of key activities, not simply the work to be conducted.

- ***Timeline***: Provide a timeline for the proposed project that includes key Clinical, CMC, Regulatory and other critical path activities, as well as major milestones.

12. IND Status *(up to 2 pages; in Part B)*
Summarize the IND status for the proposed therapeutic candidate. Describe any clinical hold issues and explain how they were/will be resolved. Clinical holds are expected to be resolved prior to the start of funding (Section V.A.3). If any amendments to the active IND are planned/required for the proposed project, provide evidence that studies supporting such amendments have been completed. Provide copies of any actual FDA correspondence in Part F.

13. Clinical Protocol Synopsis *(up to 8 pages in Part B Section 3)*
Using the CIRM Clinical Protocol Synopsis template, provide a synopsis of the proposed clinical study (up to 8 pages). A copy of this template has been provided as Sample C. In Part G provide the final full clinical protocol as well as a summary of any protocol amendments and changes that that have been made.

14. Manufacturing Plan Synopsis *(up to 6 pages in Part B Section 4)*
Using the CIRM Manufacturing Plan Template, summarize the manufacturing strategy to support the proposed clinical studies. A copy of the template has been provided as Sample D.

15. Principal Investigator (PI), Development Team and Leadership Plan *(up to 2 pages; in Part B)*
Describe the leadership plan and organizational structure of the development team. List the key members (including consultants) and indicate their roles. Describe the plan for functional area leadership and management (including: clinical, clinical operations, regulatory, CMC, translational research). Indicate who will have responsibility for regulatory and safety filings; data collection and monitoring; and quality control. Describe the plan for oversight of CMOs/CROs. Indicate Applicant and, if applicable, Partner roles and responsibilities; describe the plan for communication, process for project decision making, and plans for resolution of potential issues or conflicts.

16. Collaborations, Assets, Resources and Environment *(up to 3 pages; in Part B)*
Provide a list of collaborators that will participate in the proposed project (includes development partner/consultants/CROs/CMOs), or plans for identification and contracting collaborations. Summarize their specific roles, expertise and experience and explain how their participation is integral to the success of the project.

Summarize the assets, know-how and expertise that the partner will provide (if applicable). If consultants or subcontractors will provide expertise or resources critical to the success of the project, summarize their credentials and relevant track records.

Provide a description of the facilities, environment(s), core services, and resources available for conducting the proposed project and discuss how the proposed project will benefit from unique features of these resources. Include a description of resources available for data storage and data management.

17. Clinical Sites *(up to 2 pages; in Part B)*
Provide a list of clinical sites for the proposed clinical trial. Provide evidence that the clinical sites have experience in conducting translational early Phase 1 and Phase 2 trials. Provide evidence that the clinical sites' projected patient enrollment plan is realistic.

18. Clinical Operation Plan (up to 2 pages; in Part B)
Summarize the plan for managing the conduct of the clinical study. Describe plans for training clinical investigators and personnel at clinical sites and the plan for oversight and monitoring of clinical sites. Indicate who will be responsible for management and sign off of clinical operations activities. A copy of this template has been provided as Sample E.

19. Intellectual Property, Licenses and Agreements *(up to 2 pages; in Part B).*
Describe intellectual property assets (patent applications, patents), including any challenges to same and pending litigation relating to same and any licenses of rights important to development of the therapeutic. Identify any potentially blocking intellectual property known to applicant.

Provide a brief summary describing the status of Material Transfer Agreements (MTA) or licensing agreements for cell lines or other materials that are critical to the development of the therapeutic candidate and describe the role of those materials in the development of the product. In Part J, provide copies of essential MTA(s), or provide term sheets or letters of intent if an MTA has not yet been entered into. If not possible, please summarize the terms and what stage negotiations are in, including whether there is a term sheet, letter of intent, or MTA or licensing agreements.

If applicable, describe the status of letters authorizing the ability to cross reference Drug, Device or Facility Master Files (DMF, FMF). If possible provide copies of authorization letters in Part I.

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

21. Due Diligence Report **(***Part D***)**
If the proposed project has undergone a due diligence analysis by a pharmaceutical/biotechnology partner resulting in an executed development agreement, or term sheet or letter of intent to enter into a development agreement, provide a summary of the scope and extent of the due diligence investigation, including a list of specific assessments, the number and expertise of personnel involved in conducting the investigation, and a summary of key outcomes.

22. Investigator Brochure *(Part H)*
Provide a copy of the Investigator Brochure for the proposed candidate therapy.

C. Application Submission Instructions

All applicable parts of the Strategic Partnership IV Award application must be submitted to CIRM no later than 5:00 PM PDT on September 9, 2014 via the Grants Management Portal. It is the applicant's responsibility to meet this deadline; no exceptions to this deadline will be made.

D. 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 5:00 PM PST on November 15, 2014. 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 of supplemental materials should be in the form of a one-page letter addressed to the Associate Director of Review 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:

- 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.
- Confirmation of funding secured from other sources
- Lifting of clinical holds on IND or IDE occurring since the application submission deadline.
- 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.
- Identification of any challenges to relevant patents; updates to and pending litigation or newly initiated litigation.

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

E. Opportunity for Clarification of Submitted Information

Critical questions raised by reviewers regarding information submitted in the application will be forwarded to applicants prior to the scientific review meeting. Applicant responses will be in writing and will be made available to the GWG before the review meeting.

IX. Schedule of Deadlines and Reviews

LOI due	5:00 pm (PDT), June 19, 2014
Applications due	5:00 pm (PDT), September 9, 2014
Supplemental Information Due	5:00 pm (PST), November 15, 2014
Scientific Review of Applications by Grants Working Group (GWG)	December, 2014
Review and Approval by ICOC/Application Review Subcommittee	Q1, 2015
Earliest Funding of Awards	Q2, 2015

X. Contacts

For information about this RFA:

Sohel Talib, Ph.D.
Senior Science Officer
California Institute for Regenerative Medicine
Email: stalib@cirm.ca.gov
Phone: (415) 396-9114

For information about the review process:

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

XI. CIRM Regulations

Grant awards made through RFA 14-03 will be subject to CIRM regulations. These regulations can be found on CIRM's website.
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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 here.

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. CIRM's IP regulations are available here.

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 here). All research conducted under this award will be expected to comply with these standards. This information can be found on the CIRM website.

CIRM expects that clinical trials will be conducted in accordance with all applicable State and Federal regulations and in accordance with CIRM's Medical and Ethical Standards.

D. California Supplier Regulation

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

E. Clinical Trial Registration

CIRM requires that any clinical trial funded under any of its funding programs be listed here. CIRM will also encourage awardees to share the results, at the completion of their studies, for the benefit of the field.

F. Loan Administration Policy

In the event that the applicant chooses to receive an award in the form of a loan rather than a grant, the Loan Administration Policy (LAP) will apply and is available here and is summarized in Appendix A. Applicants should be advised that with respect to any and all RFAs, the IP and Industry Subcommittee of CIRM's board might elect to adopt terms other than the guidelines set forth in the LAP.

XII. Confidentiality of Submissions to CIRM

CIRM protects the confidential information it receives from applicants and grantees to the maximum extent permitted by law. That protection is embodied in a number of laws and policies, described below, and applies to the confidential information submitted by all applicants and grantees. CIRM does not enter into separate non-disclosure agreements with individual applicants or grantees.

A. CIRM Employees

CIRM employees are subject to the confidentiality requirements identified in a CIRM policy known as the "Incompatible Activities Statement." By law (Cal. Gov. Code § 19990) state employees are prohibited from engaging in activity identified by their employing agencies' Incompatible Activities Statements. CIRM employees are also subject to the confidentiality provision in the CIRM Employee Handbook. All employees sign statements acknowledging receipt of the Incompatible Activities Statement and the CIRM Employee Handbook.

Excerpt from Incompatible Activities Statement:

No employee shall utilize his or her status as a CIRM employee to acquire access to confidential information other than on behalf of the CIRM.

Additionally, no employee shall use such information for private gain or advantage or provide confidential information to persons to whom issuance of this information has not been authorized.

Excerpt from Employee Handbook:

All records and information relating to CIRM and its activities are confidential and employees must, therefore, treat all matters accordingly. No CIRM or CIRM related information, including without limitation, documents, notes, files, records, oral information, computer files or similar materials (except in the ordinary course of performing duties on behalf of CIRM) may be removed from CIRM without the President's authorization. Additionally, the contents of CIRM's records or information otherwise obtained in regard to CIRM activities may not be disclosed to anyone, except where required for an official purpose or by law. Employees must not disclose any confidential information, purposefully or inadvertently through casual conversation, to any unauthorized person inside or outside CIRM. Employees who are unsure about the confidential nature of specific information must ask their supervisor for clarification. Employees will be subject to appropriate disciplinary action, up to and including dismissal, for purposefully or accidentally, revealing information of a confidential nature.

B. Clinical Development Advisory Panel

Members of CIRM's Clinical Development Advisory Panel (CDAP) sign contracts that include the following provision:

Advisor shall keep confidential any information provided by CIRM or any information conveyed orally to Advisor by CIRM with oral notification of its confidentiality (the "Confidential Information"). Advisor agrees to maintain the secrecy of CIRM's Confidential Information and agrees not to use it except in performing the Services under this Agreement and not to disclose it to anyone outside CIRM or anyone within CIRM's organization who does not have a need to know it to perform under this Agreement. This non-disclosure provision shall not apply to any of the following:

1. Information, which Advisor can demonstrate by written records, was known to him or her prior to the effective date of this Agreement;
2. Is currently in, or in the future enters, the public domain other than through a breach of this Agreement or through other acts or omissions of Advisor; or
3. Is obtained lawfully from a third party.

C. Grants Working Group

The Grants Working Group (GWG) reviews grant applications. All members sign statements guaranteeing confidentiality, at the time of their appointment, and again prior to accessing application materials for each grant round.

D. Public Records Act

As a state agency, CIRM is required to allow public access to certain categories of documents held by the agency. The Public Records Act (California Government Code section 6250 et seq.) exempts certain categories of documents from public disclosure. As relevant here, agencies are not required to release trade secrets, as defined by section 3426.1(d) of the Civil Code:

"Trade secret" means information, including a formula, pattern, compilation, program, device, method, technique, or process, that (1) Derives independent economic value, actual or potential, from not being generally known to the public or to other persons who can obtain economic value from its disclosure or use; and (2) Is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

In addition, CIRM operates under special Public Records Act exemptions included in Proposition 71, the ballot initiative that created CIRM. Proposition 71 (Health & Safety Code, sec. 125290.30(e)(2)(B)-(C)) exempts from disclosure:

1. Records containing or reflecting confidential intellectual property or work product, whether patentable or not, including, but not limited to, any formula, plan, pattern, process, tool, mechanism, compound, procedure, production data, or compilation of information, which is not patented, which is known only to certain individuals who are using it to fabricate, produce, or compound an article of trade or a service having commercial value and which gives its user an opportunity to obtain a business advantage over competitors who do not know it or use it.

2. Prepublication scientific working papers or research data.

Sample A: CIRM MAJOR MILESTONES TEMPLATE

Instructions: The text below shows ***example*** milestones. To fill out the template, ***delete the example text*** and type in your own project milestones, success criteria, projected completion dates and any comments. Indicate Progress versus Go /No Go milestones. Please note: Major milestones are grouped by project year and are numbered **consecutively**.

Year 1 Milestones

	Milestone	Target completion date	Progress or Go/No Go	Comments, & Potential Risks to Timeline
CMC	1. Manufacture of the first patient product Success Criteria: Product meets specifications	Y1 Q1	Go/No Go	Assumes availability of cGMP reagents and vector if applicable
	2. Complete manufacture of patient product for Cohort 1 Success Criteria: Product meets specifications	Y1Q2	Progress	
	3. Manufacture of patient product for Cohort 2 Success Criteria: Product meets specifications	Y1 Q4	Progress	
Clinical/ Regulatory	4. Initiate first Clinical site Success Criteria: Site initiated enrolling	Y1Q1	Progress	
	5. First subject dosed Success Criteria: No treatment related SAE	Y1Q1	Progress	
	6. Complete enrollment and dosing of cohort 1 or 20% of total subjects in trial Success Criteria: No treatment related SAE	Y1Q2	Progress	
	7. Complete scheduled DMC/DSMB review Success Criteria: Continue clinical trial	Y1Q3	Go/No Go	
	8. Complete enrollment and dosing of cohort 2 or 40% of total subjects in trial Success Criteria: No treatment related SAE	Y1Q4	Progress	
	9. Complete scheduled DMC/DSMB review Success Criteria: Continue clinical trial	Y1Q4	Go/No Go	

Year 2 Milestones

	Milestone	Target completion date	Progress or Go/No Go	Comments & Potential Risks to Timeline
CMC	10. Complete product manufacturing for Cohort 3 Success Criteria: Product meets specifications	Y2 Q1	Progress	Assumes Year 1 activities and milestones are met
Pharm/tox				
Clinical/ Regulatory	11. Complete enrollment and dosing of cohort 3 or 60% of enrolled subjects in the trial Success criteria: No treatment related SAE 12. Complete scheduled DMC/DSMB review Success Criteria: No safety issues	Y2Q3 Y2Q4	Progress Progress	

Year 3 Milestones

	Milestone	Target completion date	Progress or Go/No Go	Comments & Potential Risks to Timeline
CMC	13. Complete product manufacture for all enrolled subjects	Y3Q1	Progress	
Pharm/tox				
Clinical/ Regulatory	14. Last subject enrolled and dosed 15. Last subject completed end point assessment visit 16. Follow up study visit completed for all subjects 17. Data analysis and summary of study results	Y3Q2 Y3Q3 Y3Q4 Y3Q4	Progress Progress	

Sample B: CIRM TARGET PRODUCT PROFILE (TPP) TEMPLATE

TARGET PRODUCT PROFILE for	
<Delete this text and type Name of your Product/Therapy here>	
INDICATION: ***Disease or condition for which your product/therapy will be indicated***	
Optimal indication and decision criteria < Delete and type your text here>	***Minimally acceptable indication and criteria*** < Delete and type your text here>
BIOLOGICAL ACTIVITY: ***Biological activity of your product/therapy***	
Optimal biological activity and decision criteria < Delete and type your text here>	***Minimally acceptable biological activity and criteria*** < Delete and type your text here>
EFFICACY: ***Proposed efficacy endpoints for your product/therapy***	
Optimal efficacy endpoints and decision criteria < Delete and type your text here>	***Minimally acceptable efficacy endpoints and criteria*** < Delete and type your text here>
SAFETY/CONTRAINDICATIONS*:* ***Potential safety risks associated with your product/therapy***	
Optimal safety profile and decision criteria <Delete and type your text here>	***Minimally acceptable safety profile and decision criteria*** <Delete and type your text here>
DOSE/REGIMEN: ***Briefly describe the proposed dose and dosing regimen of your product/therapy.***	
Optimal dose and dosing regimen and decision criteria <Delete and type your text here>	***Minimally acceptable dose and dosing regimen and decision criteria*** <Delete and type your text here>
DOSAGE FORM/ROUTE OF DELIVERY: ***Briefly describe the proposed dosage form and route of delivery for your product/therapy.***	
Optimal dosage form and route of delivery and decision criteria <Delete and type your text here>	***Minimally acceptable dosage form and route of delivery and decision criteria*** <Delete and type your text here>

Sample C: CIRM CLINICAL PROTOCOL SYNOPSIS TEMPLATE

STUDY TITLE
Provide full title of the study
CLINICAL PHASE
Specify clinical phase (1, 2a)
STUDY OBJECTIVES
Provide a brief description of the study objectives e.g., why is the study being done, what is the intent? E.g., safety, feasibility *Primary Objectives:* *Secondary Objectives:* *Exploratory Objectives:*
STUDY RATIONALE
Summarize the rationale for testing the proposed therapy
STUDY POPULATION
Briefly describe the study population and explain the rationale for choosing this population
MAIN INCLUSION/EXCLUSION CRITERIA
Specify the main inclusion/exclusion criteria and explain the rationale.
PRIMARY ENDPOINT (S)
Describe the Primary Endpoint(s) and the set of measurements used to address the objectives
SECONDARY & EXPLORATORY ENDPOINTS
Describe the Secondary & Exploratory Endpoint(s) and measures that will address them
STUDY DESIGN
Summarize the study design, including type of study, number of arms, controls or comparators
SUBJECT NUMBER
Provide the total number of study subjects, the number per study arm, and justification
TREATMENT DURATION
Specify the length of the treatment period

Sample C: CIRM CLINICAL PROTOCOL SYNOPSIS TEMPLATE (cont.)

DURATION OF FOLLOW UP
Specify the length of the protocol-specified follow up period
DOSE LEVEL (S) AND DOSE JUSTIFICATION
Specify the dose level(s), number of doses, and dosing frequency. Summarize how dosing was determined
ROUTE OF DELIVERY
Specify how the doses will be delivered
DATA and SAFETY MONITORING PLAN (DSMP)
Summarize the Data and Safety Monitoring Plan. Describe measures that will be implemented to minimize risk to study subjects e.g. specific inclusions/exclusions; plans to ensure medical intervention in the case of an adverse event for subjects; plans for surveillance, detection and management of specific adverse events that might or could occur; potential use of an Independent Safety Monitor or Data Safety Monitoring Board (DSMB)
STOPPING RULES
Specify stopping rules
IMMUNE MONITORING & IMMUNOSUPPRESSION
Describe and justify the plan for immunosuppression and immune monitoring (if applicable)
SUPPORTING STUDIES
Summarize supporting studies that are part of this clinical study (e.g. imaging, biomarker analyses, cell phenotyping, genotyping, gene expression analyses) that will provide critical additional data to address the objectives of this RFA or inform decisions on continued clinical testing. Include: *Objectives and rationale* *Sample collections (specify type, frequency)* *Testing methodology* *Data analysis* *Special considerations*
ASSAYS/METHODOLOGIES
Briefly describe any specialized assays or methodologies that will be used in this clinical study or supporting study/studies. (Provide a more detailed summary of assay methods and summarize assay qualification/validation in Part D). Indicate where specialized testing will be conducted
STATISTICAL ANALYSIS PLAN
Summarize the Statistical Analysis Plan or describe how the data will be analyzed

Sample C: CIRM CLINICAL PROTOCOL SYNOPSIS TEMPLATE (cont.)

OUTCOME CRITERIA
Describe criteria that would define whether you would or would not move forward with the subsequent development plan, based upon primary and designated secondary objectives
RISKS
Identify potential risks and mitigation strategies (e.g. need for and risks associated with long term immunosuppression)
CLINICAL SITES
Indicate the number of clinical sites that will participate in the study. Summarize the criteria for site selection. Provide a list of proposed sites with a brief description of the site's experience and capabilities in the conduct of clinical research.
CLINICAL OPERATIONS PLAN
Summarize the plan for managing the conduct of the clinical study. Describe plans for training clinical investigators and personnel at clinical sites and the plan for oversight and monitoring of clinical sites. Indicate who will be responsible for management and sign off of clinical operations activities.
ENROLLMENT
Describe the enrollment strategy and provide a timeline showing enrollment projections Describe plans for inclusion of women and minorities
LONG TERM FOLLOW UP
Describe requirements and plans for long term follow up and indicate how these will be supported
TIMELINE
Provide a timeline for completion of the study and indicate relevant milestones

Sample D: CIRM MANUFACTURING PLAN SYNOPSIS TEMPLATE

TEST ARTICLE
Describe the Test Article
STARTING CELL
Specify starting cell line or cellular source
MANUFACTURING PROCESS
Provide a brief description of the manufacturing process *Provide a flow diagram of the process from starting cell source to final test article* *Describe the plan for shipment of released lot from the manufacturing facility to clinical sites and describe the steps that will be performed at the clinical site*
PROCESS DURATION
Specify the duration of a manufacturing run and time required to test and release a lot
PRODUCT RELEASE
Provide a list of the product release assays and acceptance criteria
IDENTITY ASSAY
Briefly describe the Identity assay(s)
POTENCY ASSAY
Briefly describe the Potency assay(s)
ADDITIONAL CHARACTERIZATION
Briefly describe any additional characterization assays routinely performed (but not required for lot release)
LOT SIZE
Specify the average lot size (number of doses/treatments)
LOT REQUIREMENTS FOR PROPOSED CLINICAL WORK
Indicate the projected number of lots needed to support the proposed clinical work
LOT FAILURE
Specify the % failure of lot release
GMP MANUFACTURING FACILITY
Indicate where GMP manufacturing of the candidate cell therapy will be performed. Describe the experience and track record of the manufacturing facility

Sample D: CIRM MANUFACTURING PLAN SYNOPSIS TEMPLATE (cont.)

RELEASE TESTING FACILITY
Indicate where Release Testing will be performed. Describe the experience and track record of the testing facility
DOSE FORMULATION AT CLINICAL SITES
Briefly describe the plan for managing product quality control at clinical sites
CMC ACTIVITIES PROPOSED FOR FUNDING
Specify all CMC-related activities proposed for funding under this RFA and indicate which activities will be funded by CIRM
RISKS
Identify potential risks (e.g. potential for clinical hold, lot failures) and mitigation strategies
TIMELINE
Provide a timeline for the manufacturing runs planned to support the proposed clinical research and indicate relevant milestones
High Level Manufacturing Process Flow Diagram
Include - Material, Unit Operations and Analytical Methods (in process and release tests) and Timeline

Sample E: CIRM CLINICAL OPERATIONS PLAN TEMPLATE

STUDY TITLE
Provide full title of the study
CLINICAL PHASE
Specify clinical phase (1, 2)
PROTOCOL FEASIBILITY ASSESSMENT
*Discuss the **medical** feasibility of the protocol, including the appropriateness of endpoints, diagnostic tests, treatments and procedures.* *Discuss the **operational** feasibility of the protocol, including patient enrollment feasibility, the level and logistics of screening required for timely enrollment, and whether tests and procedures are logical and can be implemented with ease.*
TRIAL LEADERSHIP AND ACCOUNTABILITY
Provide a brief description of the operational plan. Indicate who will have accountability for, and ownership of, key tasks and study deliverables. Indicate who will lead clinical operations and have overall accountability for trial execution.
MEDICAL MONITORING PLAN
Describe the medical monitoring plan for the trial; Indicate who will provide medical input to sites and how medical review of the database will be performed
SAFETY MONITORING PLAN
Describe the plan for safety monitoring; including SAE processing and reporting, and DSMB review.
QUALITY MANAGEMENT PLAN
Describe the plan to ensure quality of the study and the study data, including adherence to the clinical protocol and to GCPs. Briefly describe SOPs and training requirements for staff. Describe the plan for monitoring the sites and for performing Site Audits during the study. Describe plans and processes for tracking and addressing protocol deviations [clinical corrective actions/preventative actions (CAPAs) plan] or breach in GCP. •
DATA MANAGEMENT PLAN
Describe the plan for development and maintenance of the Data Base. Include a brief description of Data Handling Procedures (include a Data Management flow diagram), Data Validation Procedures and the process for Data Review and query resolution.
CRO SELECTION AND OVERSIGHT – as applicable
Describe the process and criteria for CRO selection and the plan and processes to provide vendor oversight. Include a description of metrics, deliverables, and the process for issue escalation. Describe the plan for performing audits of CRO's and Third-party service providers.

Sample E: CIRM CLINICAL OPERATIONS PLAN TEMPLATE (cont.)

SELECTION OF CENTRAL AND SPECIALTY LABS
Describe the criteria and process for selection and management /oversight of central and specialty labs and indicate who on the sponsor team will be responsible.
CLINICAL SITE SELECTION CRITERIA
Describe the criteria for selection of clinical sites. Indicate how sites will be vetted for capabilities, resources and processes.
PATIENT RECRUITMENT PLAN
Describe the patient recruitment plan. Discuss risks and plans/strategies to mitigate slower than anticipated enrollment.
STUDY-SPECIFIC COMMUNICATION PLAN
Describe the communication plan to ensure effective communication of project status and key decisions to team members at the sponsor organization, CRO's/ vendors and participating sites.
RANDOMIZATION, INTERIM ANALYSIS AND UNBLINDING PLAN – as applicable
Describe how randomization will be conducted. Describe plans for conducting interim analysis (if applicable) in accordance with the Statistical Analysis Plan. Describe the plan for unblinding.
STATISTICAL ANALYSIS PLAN
Summarize the Statistical Analysis Plan or describe how the data will be analyzed
TECHNOLOGY TRANSFER TO CLINICAL SITE PLAN
Describe the plan for cell processing and formulation of the final test article at the clinical site. Briefly describe the SOPs, Source documents, CRF for processing and training requirements for staff.

Appendix A: LOAN INFORMATION

Loan Terms: As stated within the body of this Request for Application, a successful applicant may choose to accept the award in the form of a grant or a loan. If the award is in the form of a Loan, the CIRM and the successful applicant will enter into a loan agreement and the Loan Administration Policy (LAP) will govern. Terms of the loan are summarized below – see here for actual regulations.

(i) Two types of Loans, Company-Backed Loans and Product-Backed Loans, are available. Company-Backed Loans are subject to repayment regardless of the success of the project, whereas a loan forgiveness mechanism is available for Product Backed Loans. No personal guarantees or collateral are required.
(ii) Term: The term of the loan will be 5 years, subject to extensions as set forth in the LAP.
(iii) Payments: All principal and interest will be due and payable at the end of the loan term, unless the repayment obligation has been forgiven or accelerated. Loans that are extended require periodic payments of interest accrued.
(iv) Interest Rate: The interest rate for the initial term of the loan shall be LIBOR plus 2%.
(v) Warrants: Loan recipients will be required to provide CIRM with warrants; the amount of such warrant coverage will depend on the type of loan requested and satisfaction of certain criteria as outlined in the LAP.
(vi) Extension of Term: Loan Recipient may extend the initial term in one year increments (provided it is in compliance with the Notice of Loan Award and LAP), subject to (a) payment of 25% of unpaid and accrued interest and (b) an interest rate increase in the amount of 1% over the rate in effect the prior year.
(vii) Loan Administration Costs: Approved for-profit applicants who accept a loan will pay for loan administration costs out of the award. If the term of the loan is extended beyond year 5, the loan recipient must pay any additional loan administration costs.

Loan applicants will be required to submit financial information. For additional information about the loan program, consult the CIRM LAP.