CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

M E M O R A N D U M

October 14, 2012

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To: Independent Citizens Oversight Committee (ICOC)
Subject: Concept Proposal for Disease Team III

Background:

This concept proposal addresses the continuation of CIRM's Disease Team Therapy Development initiative. This program provides funding support for preclinical development and early clinical trials, and targets CIRM's key clinical goals articulated in the Scientific Strategic Plan (May 2012) http://www.cirm.ca.gov/files/PDFs/Publications/2012CIRMstratplan.pdf.

The Disease Team initiative was created to encourage researchers to work in multi-disciplinary teams, assembling all the skills necessary to complete key preclinical research and development activities. CIRM has awarded 2 prior Disease Team rounds (RFA 09-01 in Oct, 2009, 14 disease teams, funding initiated 2010; and recently, RFA 10-05 in Sept 2012, 11 disease teams, funding later in 2012 and early 2013), in multiple therapeutic areas. With advancing science in the field, subsequent rounds of Disease Team Awards have addressed activities at a more mature stage in the therapy development process. For example, the first round of disease teams had as their goal filing an approvable IND with the US Food and Drug Administration (FDA) to enter human clinical trials. The second round of disease teams added the aim of completing early phase clinical trials. This third round of disease teams will focus on mature projects that can complete early phase clinical trials within the planned 4 year project period.

CIRM actively manages these milestone-driven disease team projects, including evaluation by CIRM's Clinical Development Advisors Panel (CDAP) at key decision points, such as the transition from IND filing to initiation of a clinical trial. Outcomes from the initial cohort of 14 teams to date include: 1 team has achieved an IND filing and has successfully competed for funding of the clinical trials; 1 project was terminated as it was not able to meet its milestones, while the remaining 12 projects are completing their CDAP assessments in moving towards their goal of filing an IND by the end of the project period in 2014. Projects in the second round are just getting underway later in 2012 and early 2013.

Concept Proposal for RFA 13-01: Disease Team III

RFA 13-01 Disease Team III is similar to Disease Team II in scope and objectives, but focuses on more mature projects. The specific modification to the most recent Disease Team Therapy Development concept is to have a single review of the research application by the Grants

Working Group with narrowing of inclusion criteria and not to include a planning award process. This modification was discussed and approved at the Science Subcommittee meeting on October 8, 2012.

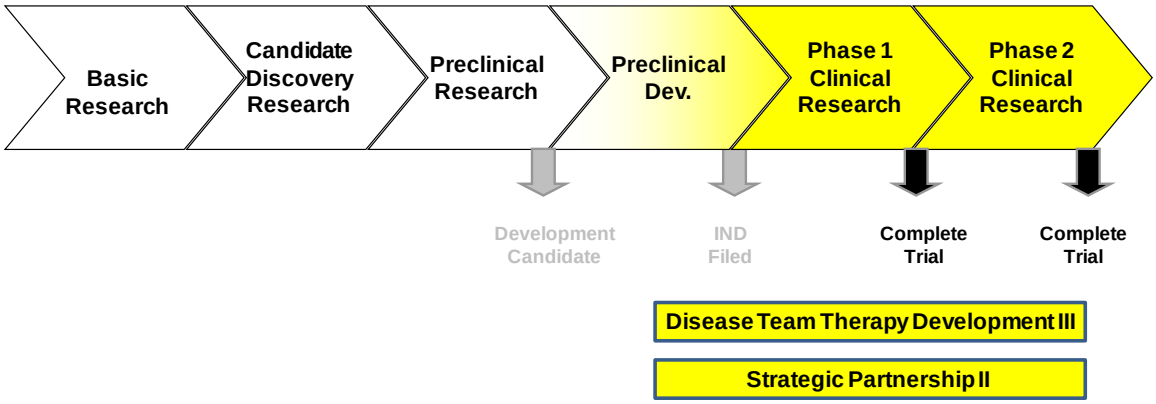
Purpose:

- Aligned with CIRM's 5 year strategic clinical objective to advance stem cell science into clinical trials to achieve therapeutic benefit to patients.

Objective:

- Completing a Phase 1 study to demonstrate preliminary safety, range of safe doses to be studied in subsequent trial, and to assess measures of biologic/clinical activity in humans; and/or
- Completing a Phase 2 clinical study conducted to evaluate efficacy of the therapeutic in a particular indication.

Scope - Activities:



CIRM intends to support meritorious projects with strong rationale and supporting data for use of the proposed therapeutic candidate in the disease or injury the applicant intends to target

The key objective of this initiative is to complete a clinical trial. This award will support the following activities:

- The conduct of early clinical trials (Phase 1 and Phase 2) for a single therapeutic entity
- IND-enabling preclinical development activities necessary to enable a phase1 clinical trial
- Supporting activities

This award excludes early research and translation activities leading up to selection of a therapeutic development candidate, pivotal efficacy studies (Phase 3), and cGMP production for pivotal efficacy studies.

Project Eligibility:

Readiness –

- Single final therapeutic development candidate chosen, for which there is a strong clinical rationale.

- Strong preclinical proof-of-concept (POC) evidence supporting use of the candidate in the target disease/injury; for example, disease modifying activity in a relevant animal model with the intended therapeutic candidate.
- For all projects proposing to start with IND-enabling studies, the applicant must have completed a pre-IND meeting with FDA. Based on the outcome of that discussion, a project should be projected to be within 12-18 months of IND filing.
- For projects ready to start a Phase 1 clinical trial, applicants must have submitted an IND package to the FDA by the LOI deadline.
- For projects ready to start a Phase 2 clinical trial, applicants must have Phase 1 data demonstrating preliminary safety in the target population.

Therapeutic Candidate –

This award will support a therapeutic candidate derived from or comprised of the following:

- pluripotent-derived cells
- allogeneic tissue-derived stem cells or progenitor cells for repair / regeneration
- stem cell-engineered functional tissues for implantation in vivo
- small molecules or biologics targeting endogenous stem cells as primary mechanism of action (in vivo) for regeneration and repair
- genetically or pharmacologically-modified HSCs

Institutional Eligibility:

- Open to all academic, not-for-profit and for profit research institutions, and combinations of these as partnerships
- Applicant may not submit substantively the same project to both the SPII and DTIII

Award information:

- CIRM is targeting up to 5 awards and proposes to commit up to $100 M under this RFA
- CIRM will fund between $5 and $20 M total costs per project for programs to develop the candidate therapeutic, for up to four years to meet one or more of the objectives of the RFA. Only in extraordinary cases is it expected that a project would be funded at the higher end of the range
- CIRM will require co-funding from the applicant

Award mechanism:

- Grant, if PI holds the IND and is from a non-profit organization
- Choice of Grant or Loan, if a for-profit organization holds (sponsors) the IND and is the applicant organization. The loan holder will be responsible for the entire award from CIRM, even if a Co-PI is from a non-profit organization.

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 that organization.

Provisional Time Table:

Post RFA 13-01	Jan	2013
LOIs due	Mar	2013
Full Applications due	May	2013
Review of Applications by Grants Working Group (GWG)	Aug	2013
Review and Approval by ICOC	Oct	2013
Earliest Funding of Awards	Jan	2014