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The state stem cell agency

Strategic Partnership IV Funding Initiative: RFA 14-03

Educational Webinar for Potential Applicants May 14, 2014

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Providing tips to help you better prepare your application – our Webinar objective

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- We will review the following:
  - Goals and intent of the RFA
  - Applicant eligibility
  - Project eligibility
  - Tips for Success
  - Review Criteria
  - Templates to guide your organization of the material
  - Contact Info – how to reach us at CIRM
- We're here to answer your questions and help better position you for success

RFA intent – attract industry

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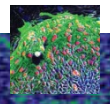
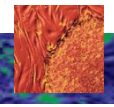
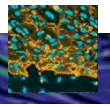
- **Purpose** of the Strategic Partnership Initiative is to attract **industry** engagement and investment in CIRM funded stem cell research
- Two key features
  - Applicants must demonstrate **Commercial Validation** to be eligible
  - **Co-funding** is a requirement
- CIRM intends to offer **repeat calls** under this initiative every 6-9 months. The focus, scope and objective may differ with each solicitation.

Key Features: RFA 14-03

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- Open to for-profit and non-profit applicants
- Only 1 application allowed per PI and 1 per organization if for-profit
- **Award**: up to $10M over 3-years for **1** project/applicant
  - $12M in extraordinary circumstances
- **Objective**: to Complete a Phase 1 or Phase 2 trial within **3-yrs**
- **Co-funding**
  - Applicant must match 100% of costs requested (1:1 match)
  - Costs requested can include direct and indirect project costs
  - Applicant match can be in form of capital or in-kind services
- Details in **RFA 14-03**

Key Differences with Previous Strategic Partnership RFA

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- Focused on mature clinical stage projects
- Only fund programs for which a complete Investigational New Drug (IND) filed by application due date (September 9, 2014)
- Complete a Phase 1 or Phase 2 trial within 3-yrs

Commercial Validation

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All applicants must provide evidence of commercial validation

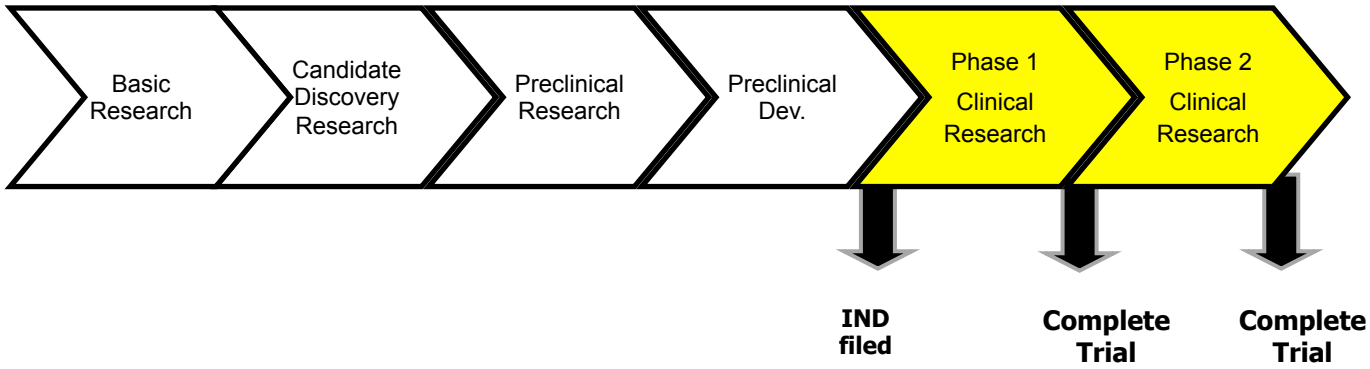
- **For-profit applicants**
  - either by financial strength
  - and/or via a collaborative research agreement with a large biotech/ pharma partner
- **Not-for-profit applicants**
  - must have a collaborative research agreement with a large biotech/ pharma partner (market capitalization of at least $500M)
- See RFA Sections V.D and VIII.A for details
- **The agreement with the Bio/Pharma** must cover co-funding and collaboration support for the proposed project (it need not be a full development agreement).

Key Dates for establishing Commercial Validation

- To establish Commercial Validation via Financial Strength
  - Submit financial statements and other documents with LOI –see Section VIII.A
- Applicants seeking to establish Commercial Validation via an **agreement** with a Bio/Pharma must have:
  - by the **LOI due date** (**June 19, 2014**), a letter from the Bio/Pharma company indicating that they are interested in co-funding the proposed project and are negotiating terms of support
  - by the deadline for Supplemental Information (**Nov 15, 2014**), a term sheet and/or letter of intent relating to the agreement
  - two weeks before the Board meeting to approve funding for Strategic Partnership IV awards (**Q1, 2015**), the fully executed agreement

Scope: RFA 14-03

SP IV is designed to capture ***mature*** programs at **Early Clinical Development** stage



- All activities to initiate and complete a Phase 1 or Phase 2 clinical trial
- Can include supporting activities such as manufacturing and potency assay development

Readiness – Eligibility Criterion

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Applicants must have:

- Single final development candidate selected
- Evidence of **preclinical POC** with the candidate in the target disease/injury
- Evidence of **IND filing** by Application deadline (September 9, 2014)
  - Applicants whose IND on clinical hold - provide both the FDA comments and plan to resolve the clinical hold no later than December 1, 2014
  - IND cleared with no clinical hold before CIRM funding

Organization Eligibility – California Presence

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- Applicant organizations must have a CA presence to be eligible
- At least 2 full-time equivalent (FTE) key personnel + 30% effort in California by the PI
- Refer to Section V,C of RFA

Therapeutic Candidate- what's in-scope

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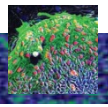
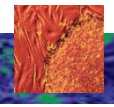
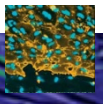
- Cell therapy derived from pluripotent stem cells
- Allogeneic tissue-derived stem cells or progenitor cells for repair/ regeneration
- Stem cell-engineered functional tissues for implantation in vivo
- A small molecule or biologic demonstrated to target **normal endogenous stem cells** in vivo as the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

What's out of scope for this round

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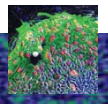
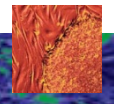
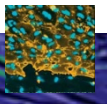
Out of Scope and Specifically Excluded:

- Unmodified 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

Tips for Success – an aid, not a promise!

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- **Start with a great idea** – we want your best ideas and best research to move forward and a strong rationale. If this program isn't of top interest for your company, you're unlikely to convince the reviewers it should be CIRM's
- **Explain how this program fits into your overall company strategy** as well as in the competitive landscape of other compounds/programs for the same target/indication
- **Preliminary data** is important – provide it!
- **Show the data**, not just your interpretation of the data – reviewers base their recommendations on the evidence, not on your hopes

Tips for Success – an aid, not a promise!

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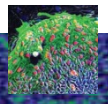
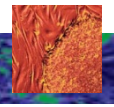
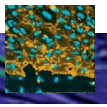
- **Describe** what and where the **risks** are, **and plans to mitigate or remove them** – it shows you are on top of the issues and are thinking of all sides; painting a rosy picture and not addressing challenges or risks weakens your application
- Address the probability of success and disease impact
- **Address commercial viability** of your proposed therapy
  - Will it be practical and feasible for patients and healthcare providers
  - What will differentiate it from other competing therapies and current standard of care
- **Address freedom to operate** and any investment you've made to ensure it

Tips for Success – an aid, not a promise!

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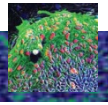
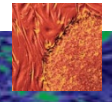
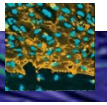
- **Milestones should be clear and important** - what are the critical experiments for that Go-No Go decision to ensure you have the "truth" about whether or not to proceed
- B**udgets should be well justified -** be good stewards of the $ and provide the rationale for what you really need to conduct the studies and answer the key questions or issues
- **Timelines should be well reasoned** – provide rational, realistic time frames

Tips for Success – read the RFA!

- **Read the RFA** – make sure you understand what's being asked and what you need to provide
  - As examples **Show:** the aspirational Target Product Profile; the overall development plan (Phase 1 clinical trial – development plan through the End- of-Phase 2; Phase 2 –development plan for pivotal trials to gain Marketing Approval); documentation that you have filed IND; addressed FDA comments and ready to start clinical trial at the time of CIRM funding; documentation that you have the legal ability to move your product forward to patients; provide a clinical trial protocol that is well-designed, has safety parameters in place for patients, and is designed to answer the key questions you need to make a decision about whether to move the product forward into later stage development

Tips for Success – an aid, not a promise!

- **Know your audience** – who are you trying to convince with your proposal – it's the reviewers with product development, disease, clinical, preclinical, manufacturing expertise and experience, and it's CIRM – know CIRM's mission and read the RFA to understand what's needed
- **Ask questions as you prepare the application** – don't guess, ask CIRM if you are unsure. All potential applicants should pick up the phone or email CIRM – let us know you are interested and let us try to help you
- **Reserve time to write the application** – a competitive application requires focus

Examples of what NOT to do

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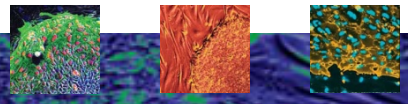
- Propose a large, multi-center, multi-national trial without any evidence you have tested your proposed product in any human
- Propose a clinical indication with no or weak rationale, that is peripheral to the company's main priorities that have much stronger scientific and clinical rationale
- Dismiss or ignore data that doesn't fit with your rationale – go over the data and explain it, state the studies you will do that can answer the question
- List completed studies without providing the data – drafts are informative and it's important to be transparent about your data
- Name a principal investigator with no or very limited product development experience in conducting or successfully guiding studies into the clinic



Examples of what NOT to do

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- Provide the idealized view, with no or minimal information on potential scientific, technical, regulatory, or clinical risks or challenges to the project and how you will address them
- Request $ millions for CRO/CMO and provide a one sentence rationale and description of what you intend to do with the $ - all activities, particularly expensive ones, require appropriate justification
- Take the published award ceiling amount and divide by the number of years to arrive at your annual budget needs
- Propose budget and cost sharing for expenses/activities outside the scope of the CIRM funded project
- Propose an unrealistically optimistic time frame – could impact on reviewers' perception of team's experience

Review Criteria to assess the application

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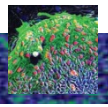
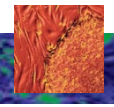
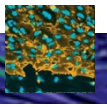
- All Applications will be evaluated by Grants Review Group in five key areas:
  - Significance and impact
  - Rationale and Risk/Benefit
  - Design and feasibility
  - Principal investigator, development team and leadership plan
  - Quality of collaborations, assets, resources and environment

Templates to guide the organization of your submission

- CIRM Major Milestones Template
- CIRM Target Product Profile (TPP)
- CIRM Clinical Protocol Synopsis
- CIRM Manufacturing Plan Synopsis
- CIRM Clinical Operations Plan Template
- Other key information you will need to provide includes:
  - Due Diligence Report
  - FDA correspondence
  - Clinical Protocol and Investigator Brochure
  - Copies of authorization for cross reference of Drug, Device or Facility master files
  - Licenses and agreements (MTAs)
  - Evidence of Commercial Validation
  - Related Business Entities Disclosure Form

CIRM's ICOC has allocated $32 million for up to 3 projects:

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Key dates to remember:

Letter of Intent due	June 19, 2014
Award Applications due	Sept 9, 2014
Supplemental Information due	Nov 15, 2014
Grants Working Group review	Dec, 2014
ICOC Consideration	Q1, 2015
Earliest Funding	Q2, 2015

Contact us if you have any questions

- **For information about this RFA:**
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