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The state stem cell agency

Disease Team Therapy Development III: RFA 13-01

Educational Webinar for Potential Applicants February 6, 2013

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Providing tips to help you better prepare your application – webinar objective

- We will review the following:
  - Goals and intent of the RFA
  - Tips for Success
  - Context of this initiative within CIRM's portfolio
  - Eligibility criteria: Therapeutic Candidate, Principal investigator, and Organization
  - Review Criteria for this RFA
  - Early Translational Allowance Pathway
  - 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's goals and intent

- **Purpose** of the Disease Team program is to advance preclinical and early clinical development of novel therapies
- **Objective** of this third call, Disease Team Therapy Development III, is to complete, in 4 years or less, an early phase clinical trial under an IND with the FDA
- Proposed projects can include preclinical IND-enabling work but must complete one or more of the following:
  - Phase 1 clinical study
  - Phase 2 clinical study
- For CIRM Early Translational awardees only: objective is to file a well-supported IND (more info on this to come)

Tips for Success – an aid, not a promise!

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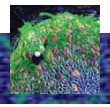
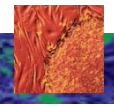
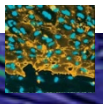
- **Start with a great idea** – we want your best ideas and research to move forward, and a strong rationale.
- **Explain your overall development strategy**, as well as other candidates for the same target/indication
- **Preliminary data** is important – provide it! Preliminary data should be using the same therapeutic candidate as you intend to use in the clinic.
- **Show the data**, not just your interpretation of the data – reviewers base their recommendations on evidence, not on the claims you make

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 novelty vs probability of success and disease impact
- Address commercial viability of your proposed therapy
  - Differentiate from potentially competing therapies and current standard of care
- Address access to any key intellectual property and/or materials or reagents necessary to use your candidate in a clinical trial.

Tips for Success – an aid, not a promise!

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- **Milestones should be clear and meaningful** - what are the critical experiments to inform Go/No-Go decision points

- B**udgets should be well justified -** be good stewards of CIRM funds and provide the rationale for what you need to conduct the proposed studies and answer the key questions or issues

- **Timelines should be well reasoned** – provide rational, realistic time frames

Tips for Success – read the RFA!

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- **Read the RFA** – make sure you understand what's being asked and be sure to address the points
  - As examples: Show the aspirational Target Product Profile; the development plan; studies to provide the evidence; knowledge of the regulatory steps; data to show strong proof of concept with your therapeutic candidate; documentation that you have discussed your product with the FDA; documentation that you have the legal ability to move your product forward to patients; provide a well designed clinical trial protocol that has safety parameters in place for patients, and is designed to answer the key questions you need to make a decision about whether to proceed into later stage development

Tips for Success – an aid, not a promise!

- **Know your audience** – who are you trying to convince with your proposal
  - Reviewers with product development, disease, clinical, preclinical, and manufacturing expertise and experience
  - 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 contact 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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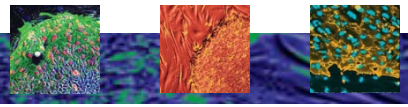
- Provide data using a different therapeutic candidate or in a different indication than for the proposed clinical trial.
  - If you change your manufacturing method, it might be a new product.
- Dismiss or ignore data that doesn't fit with your rationale – explain the data and state studies you will do to answer the question.
- List completed studies without providing the data – be transparent about your data.
- Name a PI with little or no product development experience in successfully moving studies into the clinic.
- Propose a clinical indication with weak rationale – pursue the most compelling indication based on the data you have.
- Propose a large, multi-center trial without any evidence that you have tested your proposed product in any human.

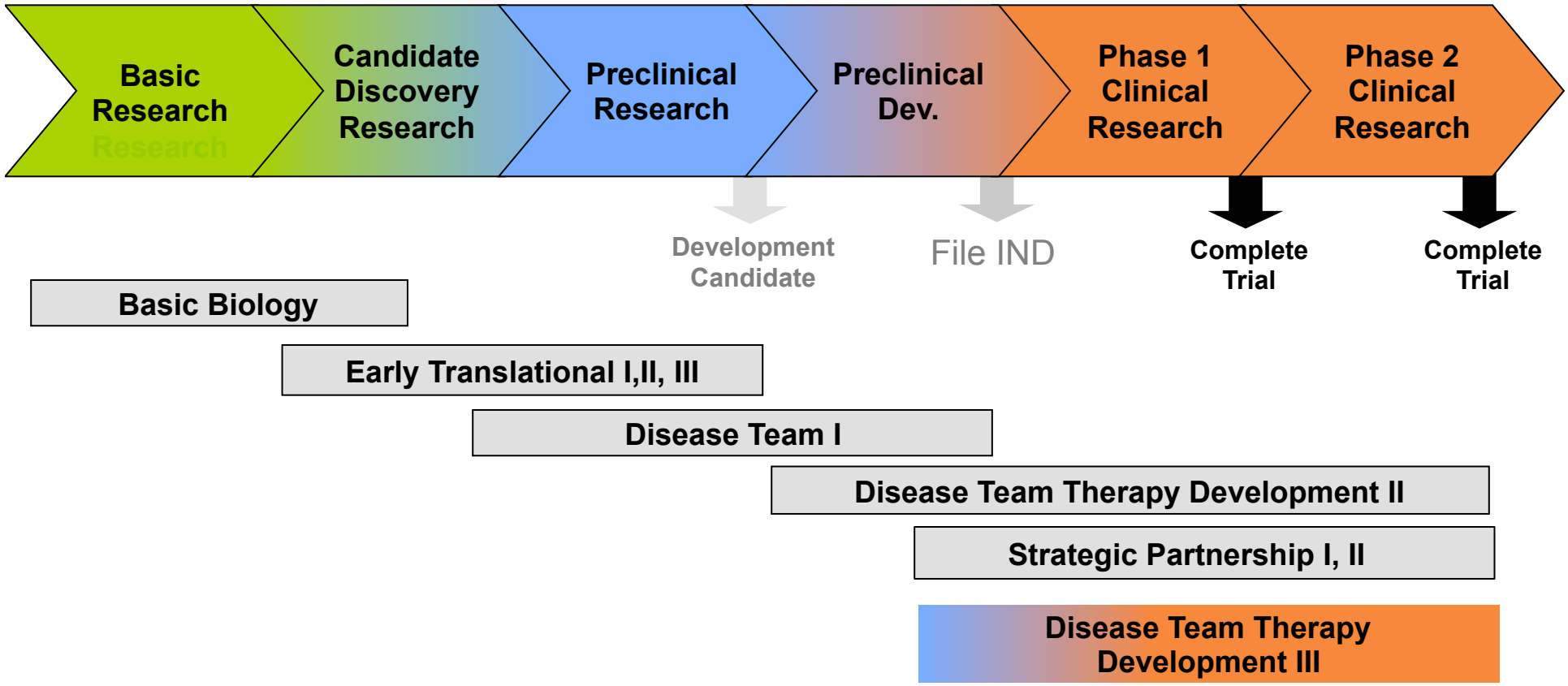


Examples of what NOT to do

- Provide the idealized view, with little or no information on potential scientific, technical, regulatory, or clinical risks or challenges to the project and how you will address them.
- Request millions for “toxicity studies” 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 a budget including expenses/activities outside the scope of the project proposed to CIRM.
- Propose an unrealistically optimistic time frame – this could affect reviewers’ perception of team’s experience.

Scope: Disease Team Therapy Development III

DTTD III is designed to capture ***mature*** programs close to/at **Early Clinical Development** stage



Readiness

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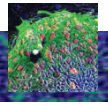
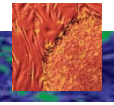
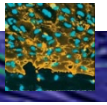
Preclinical Stage Projects must have:

- Single therapeutic development candidate selected.
- Preclinical proof-of-concept (POC) in target disease/injury with the proposed therapeutic candidate.
- Pre-IND meeting with FDA should be completed by May 15, 2013.

Clinical Stage Projects must have:

- IND filed by March 13, 2013

Therapeutic Candidate Eligibility

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- A cell therapy derived from human pluripotent stem cells
- Allogeneic adult stem cells or progenitor cells for repair / regeneration, except for those that are out of scope
- Genetically- or pharmacologically-modified hematopoietic stem cells for repair and/or regeneration
- Tissue engineered functional tissues for implantation in vivo (e.g. utilizing a cell scaffold or biomaterial in combination with a stem or progenitor cell)
- Small molecule or biologic (e.g. antibody, protein) demonstrated to target normal endogenous stem cells as the primary mechanism of action (in vivo) for regeneration and repair
- Any therapeutic candidate developed under a Disease Team I (RFA 09-01) award

Out of Scope Approaches

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Out of Scope and Specifically Excluded:

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

Eligibility Criteria for PI and Organizations

- PIs must have an MD, PhD or equivalent degree and be authorized by applicant organization to conduct the proposed research in California
  - PI is an employee of applicant organization with demonstrated expertise in product development and in managing clinical research programs
  - Documented commitment from applicant organization to provide resources sufficient to carry out research
- Applicant organization must have a CA presence to be eligible; the extent of that CA presence determines the scope of CIRM funding – Refer to Section V.B of RFA

Review Criteria

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- Applications will be evaluated by Grants Review Group in 8 key areas:
  - Significance and impact
  - Scientific Rationale and Risk/Benefit
  - Therapeutic Development Readiness
  - Design and Feasibility
  - PI, Development Team and Leadership Plan
  - Budget
  - Collaborations, Assets, Resources and Environment
  - Intellectual Property and Licenses

Co-Funding Expectation

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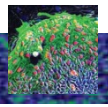
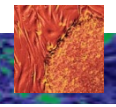
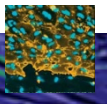
- If you are proposing to conduct a clinical trial using a small molecule or biologic (e.g. antibody, protein) you must:
  - Match 25% of the CIRM-requested funds for the costs associated with the clinical trial
    - See Section III.B in RFA for more information
    - Amount of required match will be calculated on the Activity Based Budget worksheet (Part D of the application)
- Cell therapy products are not required to provide matching funds, although it is encouraged

Early Translational Allowance Pathway

- To ensure a pathway to success for current CIRM-funded projects, ET awardees can apply with the goal of filing an IND within 4 years.
- Available ONLY to CIRM Early Translational awardees who have completed milestones and activities of the ET award to achieve a well-supported DC (See Section V.G).
- Any therapeutic approach developed under an ET award is eligible.
  - Except: a proposed small molecule or biologic must target normal endogenous stem cells as the primary MOA (in vivo) for regeneration and repair

Collaborative Funding Partners

Country	Agency	For more info
United Kingdom	Medical Research Council	Appendix B
China	Ministry of Science and Technology	Appendix C
United States	National Institutes of Health	Appendix D
Andalusia, Spain	Andalusian Initiative for Advanced Therapies	Appendix E

- See Section IV in the RFA
- For general questions about the CFP program contact Ian Sweedler (isweedler@cirm.ca.gov)
- For questions regarding specific CFPs and their requirements see contact information in the appropriate appendix

Application requirements

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Required parts to the application, as seen on page 21 of the RFA:

Part	Description	General Applicants	ET Allowance Pathway Applicants
A	Application Information Form	Required	Required
B	Proposal	Required	Required
C	Biographical Sketches	Required	Required
D	Activity Based Budget	Required	Required
E	Regulatory Correspondence	Required	Required, if any
F	Clinical Protocol	Required	Not applicable
G	Investigator Brochure	Required	Not applicable
H	Authorization for Cross Reference	Required, if applicable	Required, if applicable
I	Licenses and Agreements	Required	Required

Templates to guide the organization of your submission

- CIRM Major Milestones Template
- CIRM Target Product Profile (TPP) Template
  - CIRM workshop on preparing a TPP available at: http://youtu.be/QK_zPmarkws
- CIRM Clinical Protocol Synopsis Template
- CIRM Manufacturing Plan Synopsis Template

CIRM's ICOC has allocated up to $100 million for up to 5 awards:

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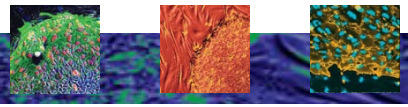
Key dates to remember:

Letter of Intent due	March 13, 2013
Award Applications due	May 15, 2013
Grants Review Group review	August 2013
ICOC Consideration	Q4 2013
Earliest Funding	Q1 2014



Contact us if you have any questions

- **For information about this RFA:**

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- **For information about the review process:**

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