CALIFORNIA'S STEM CELL AGENCY

The state stem cell agency

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Preclinical Development I Awards: RFA 14-02

Educational Webinar for Potential Applicants
May 13, 2014

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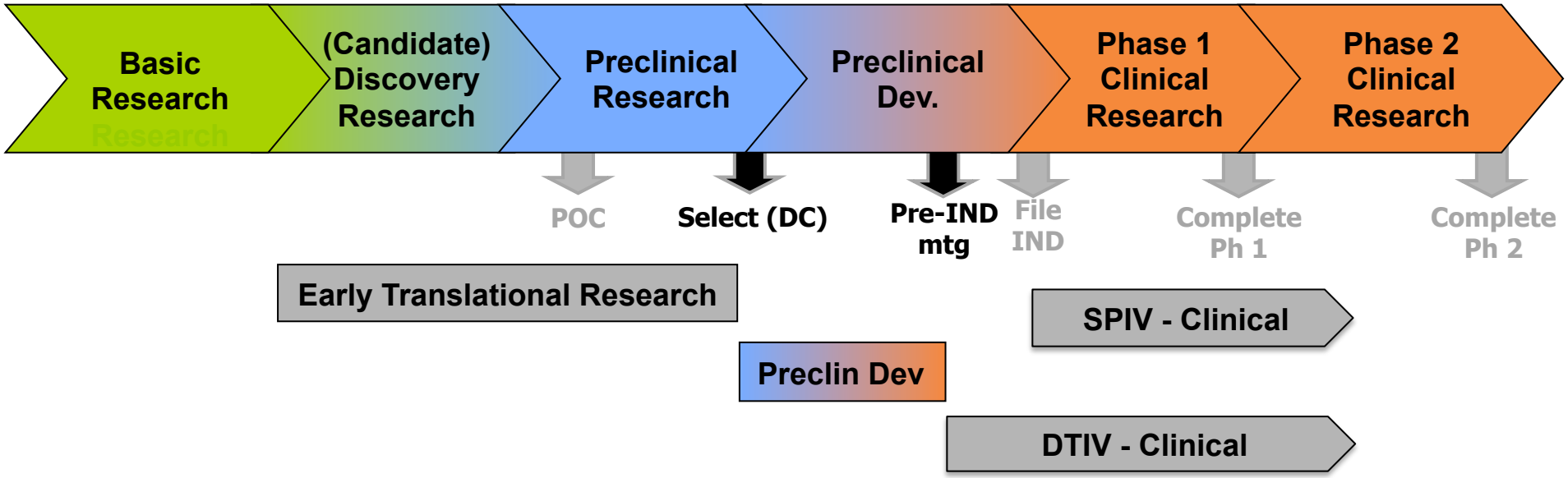
Webinar Objective: To provide information about RFA 14-02, Preclinical Development I Awards

- To discuss today:
  - Purpose, Objectives and Scope of the RFA
  - Funding Information
  - Eligibility Criteria
  - Collaborative Funding Partners
  - Review Criteria
  - Application Information
  - Tips for Success
  - Schedule of deadlines and reviews
  - Contact information for further questions

RFA 14-02: Intent



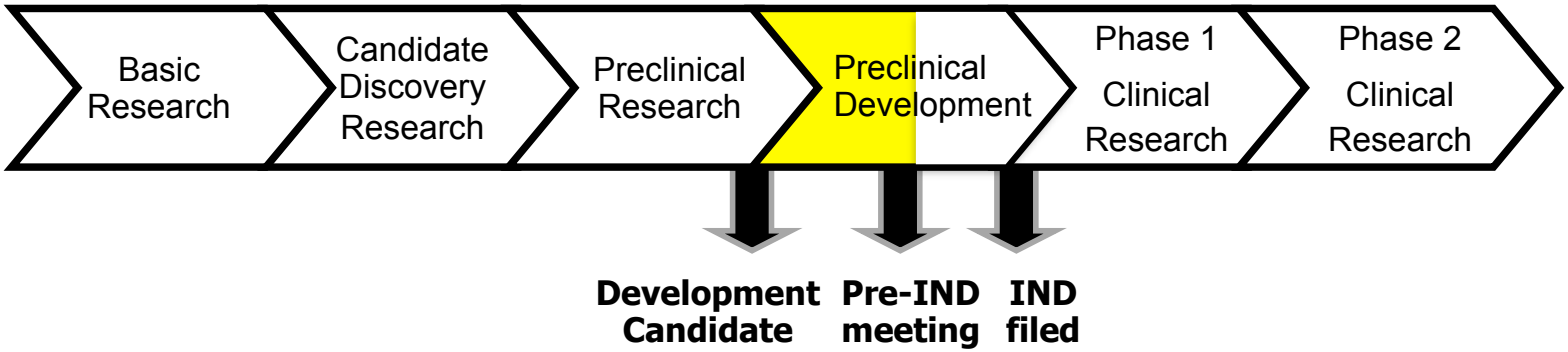
Advance toward the clinic the most promising and competitive projects that address significant unmet medical needs from

- CIRM's translational pipeline
- New translational projects (with co-funding)

RFA 14-02: Purpose

- Support CIRM's mission for the discovery and development of stem cell therapies.
- Provide a mechanism for successful CIRM-funded stem-cell based translational projects, and those promising projects external to CIRM that have matching co-funding, to advance toward the clinic.
- Fund the early preclinical development activities needed to position projects to move smoothly through pivotal IND-enabling studies, IND filing and First-In-Human clinical studies, and ultimately, to be competitive for future funding and/or to attract partners.

RFA 14-02: Objective



Objective: To carry out all activities needed to conduct, within 30 months, a well-prepared pre-IND meeting with the FDA, during which readiness is demonstrated to:

1) Manufacture GMP product to support pivotal preclinical safety studies and a Phase 1 trial.
2) Carry out agreed-to pivotal safety studies with GMP product

RFA 14-02: Funding Information:

- Total Program Costs: up to $40 MM
  - Estimate 5 - 8 awards
- Award Amount
  - Up to $5 - 8 MM per project
  - Under exceptional circumstances up to $10 MM
- Award Term
  - 2.5 years (30 months)
- Award mechanism
  - Grant (non-profit applicant organization)
  - Grant or Loan (for-profit applicant organization)

RFA 14-02: Co-Funding

- If candidate was identified with non-CIRM funding:
  - One to one (100%) matching co-funding required.
  - Matching funds may be from applicant, an industry partner, or other funding source.
  - Matching may be in the form of capital or in-kind services.

- If candidate was identified with CIRM funding, the project is eligible for full funding from CIRM for this award.

RFA 14-02:
Activities to prepare for a pre-IND meeting

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In Scope

- ❑ Develop a scalable stage-appropriate GMP manufacturing process and associated analytics
- ❑ Optimize and select dose(s), regimen and route of administration in models
- ❑ Complete pharmacokinetic, pilot safety (immunogenicity, tumorigenicity) and mechanism-of-action studies
- ❑ Select FIH target indication and prepare clinical development plan including draft protocol for trial
- ❑ Conduct pre-pre-IND and pre-IND meetings

Out of Scope

- ❑ Research to identify a Development Candidate.
- ❑ Pivotal IND-enabling safety studies.
- ❑ cGMP Production for preclinical or clinical studies.
- ❑ Clinical Studies

See RFA for details.

RFA 14-02: Development Candidate Eligibility

Must be a single candidate derived from or targeting stem cells.

Eligible	*Ineligible*
❑ Pluripotent-cell derived	❑ Unmodified HSC or MSC
❑ Allogeneic or autologous adult stem or progenitor cells (with exceptions)	❑ Minimally manipulated bone marrow or cord blood cells
❑ Genetically- or pharmacologically modified HSC or MSC	❑ Small molecules or biologics not targeting endogenous stem cells
❑ Engineered tissues derived from stem cells	
❑ Small molecule or biologic that targets normal endogenous stem cells	

See RFA for details.

RFA 14-02: Eligibility - DC Readiness

- Convincing, reproducible disease-modifying activity in relevant models.
- Preliminary data evaluating dosing, safety and mechanism of action.
- Research assays to characterize identity, purity, activity.
- Methods for research grade production of DC.

See RFA for details.

RFA 14-02: Collaborative Funding Partners

For projects in which the candidate was identified during a CIRM/Collaborative Funding Partner (CFP) collaboration, CIRM will work with the CFP to determine whether collaborative funding can be available for this award.

RFA 14-02: Review Criteria

- Applications will be evaluated for scientific merit by the GWG in five key areas:
  - Significance and Impact
  - Scientific Rationale and Preclinical Development Readiness
  - Design and Feasibility
  - Principal Investigator, Development Team and Leadership Plan
  - Collaborations, Assets, Resources and Environment

RFA 14-02: Priorities

Priority is given to projects that:

1) Propose therapies derived from pluripotent stem cells or directly reprogrammed cells.
2) Are potentially transformative and address unmet medical needs.
3) Have at least 25% co-funding (if from CIRM translational project).
4) Have 100% matching co-funding from industry (if project is new to CIRM).

Priority status is taken into consideration when a funding choice must be made between similar quality proposals.

RFA 14-02: Application Requirements

- The application for this RFA consists of up to six parts:

Application Part	Description	Required?
A	Application Information Form	Yes
B	Proposal	Yes
C	Biographical Sketches	Yes
D	Activity Based Budget	Yes
E	Licenses, Co-Funding and Material Transfer Agreements	Yes, if applicable
F	Regulatory Correspondence	Yes, if applicable

RFA 14-02: Templates

- Four templates for required elements of the application are provided at the end of the RFA:
  - Preclinical Development Award Milestones Template
  - Target Product Profile (TPP) Template
  - Preclinical Studies Summary Template
  - Clinical Trial Synopsis Template

Resources to understand the purpose of and how to develop a TPP:

- FDA Guidance: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm080593.pdf
- CIRM Workshop: http://www.cirm.ca.gov/our-progress/video/target-product-profile-ellen-feigal-2011-cirm-grantee-meeting

RFA 14-02: Tips for Success

- Provide key preliminary data showing evidence of candidate “readiness”.
- Explain the rationale for developing this product. What unmet need will it fill, and how will it be differentiated from competing therapies?
- Describe potential risks and plans to mitigate those risks.
- Address access to key intellectual property that would be necessary to use the candidate in a clinical trial.

RFA 14-02: Tips for Success

- Know your audience:
  - GWG: reviewers with product development, disease, clinical, preclinical, and manufacturing expertise.
  - CIRM: know CIRM's mission and read the RFA carefully.
- Ask questions as you prepare the application.
- Produce well-reasoned budgets with a clear rationale for expenditures.
- Provide realistic time lines that have mitigation strategies.
- Propose milestones that are clear and meaningful.

RFA 14-02: Schedule of Deadlines, Reviews

Key dates to remember:

Schedule of CIRM Deadlines and Reviews	Date
Letters of Intent due	5:00 pm (PDT), Thursday, June 5, 2014
Full Applications due	5:00 pm (PDT), Thursday, August 14, 2014
Review of full Applications by Grants Working Group (GWG)	Q4, 2014
Review and Approval by ICOC	Q1, 2015
Earliest Funding of Awards	Q2, 2015

RFA 14-02: Contact Information

- **For information about this RFA:**

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

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- **For information about Collaborative Funding Partnerships:**

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