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The state stem cell agency

CIRM Strategic Partnership III Awards: RFA 13-03A Grants Working Group Recommendations

Ingrid Caras, PhD

May 29, 2014

Agenda Item 8

Purpose: Strategic Partnership Initiative

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- Purpose of the SP Initiative is to attract ***industry*** **engagement and investment** in CIRM-funded stem cell research
- To

  (i) provide a source of **co-funding** in the early stages of development

  (ii) enhance the likelihood that CIRM-funded projects will obtain **follow-on financing**

  (iii) enable CIRM-funded projects to access **development expertise** within large pharma/biotech partners

Unique Features: Strategic Partnership Initiative

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1. Requires applicants to demonstrate **Commercial Validation** i.e. to show they have **financial capacity** to move the project through development

as evidenced by:

(i) financial strength based on investments and liquid assets

OR

(ii) a research/development agreement with a large pharma/biotech company

2. Requires applicants to provide **co-funding** for proposed project

Background: Strategic Partnership Initiative

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- Strategic Partnership Initiative
  - Approved by ICOC Oct, 2011
  - Amended Sep, 2012
- Current concept directs CIRM to implement the Initiative via **RFA process**
  - Solicitations every 6-9 months
- **RFA-13-03A**: **Strategic Partnership III** Awards
  - **Third** solicitation under this initiative
  - Award amount: Up to $10M over 4-years per award
    - $15M in extraordinary circumstances
  - Up to $80M allocated

Objective of Strategic Partnership III RFA

- Objective of SP III Award is completion within 4-years of an early stage **Clinical Trial**
  - Phase 1 or Phase 2
  - The 4-yr project can include preclinical **IND-enabling** work but all applicants must be able to complete a clinical trial

- Aligned with CIRM's **5 year strategic goal** to attract industry engagement and investment in CIRM funded stem cell research
- Aligned with CIRM's **5 year strategic clinical objective** to advance stem cell science into clinical trials to achieve therapeutic benefit to patients

RFA Priorities

- Proposals aimed at furthering development of **successfully completed CIRM-funded projects**.
- Proposals from applicants that have secured a **development agreement** with a large biotech/pharma company.
- Proposals that include a clinical study that could demonstrate **clinical proof-of-concept** if successful.
- Proposals that cannot, or are unlikely to, receive timely or sufficient federal funding.

Scope of Strategic Partnership III

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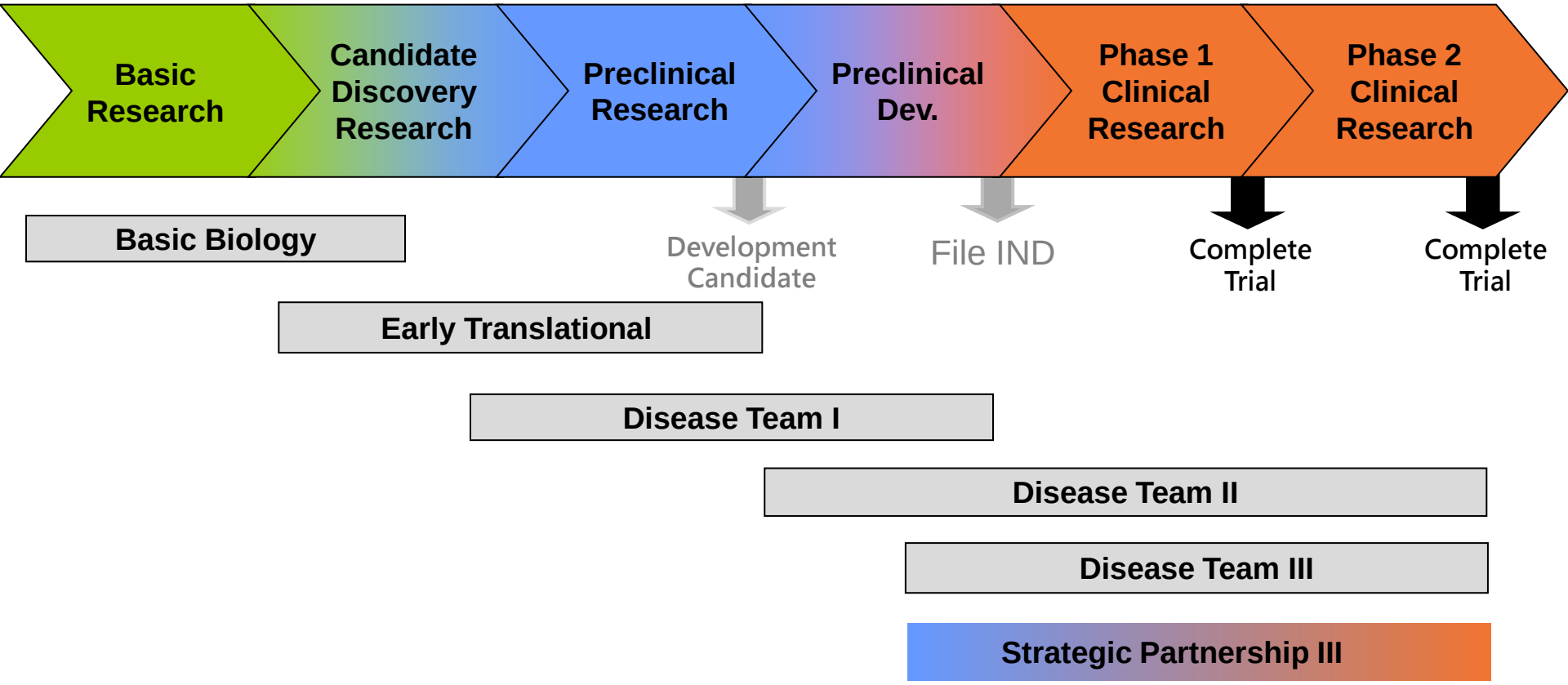
Strategic Partnership III is designed to capture **mature** programs close to/at **Early Clinical Development** stage



Review Criteria

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1. Significance and Impact
2. Scientific Rationale and Risk/Benefit
3. Design and Feasibility
   - Development plan
   - Preclinical plan
   - Manufacturing strategy
   - Clinical Trial
4. Principal Investigator (PI), Development Team and Leadership Plan
5. Collaborations, Assets, Resources and Environment

GWG Expertise

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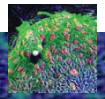
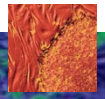
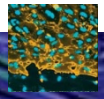
- Each application was evaluated by multiple reviewers with **specialized expertise** in key areas:
  - Therapy development
  - Regulatory process
  - Preclinical Pharmacology/Toxicology
  - Manufacturing
  - Clinical trial design
  - Clinical operations
  - Disease expertise in the target disease indication
- GWG Review meeting Feb, 2014

Scientific Merit Scoring

- 100 is highest and 1 is lowest score possible
- Scores are determinative

Tier	Score	Status
1	75-100	Recommended for funding
2	65-74	Moderate science or no consensus, Suitable for Programmatic
3	1-64	Not Recommended for Funding

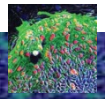
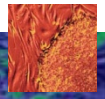
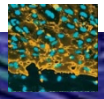
Summary: Strategic Partnership III GWG Review

- **6** applications met Commercial Validation & other eligibility requirements and were reviewed
- **5** were from Industry applicants; 1 was Academic with Industry Partner

Tier	Status	# SPIII Applications
Tier 1	Recommended	2
Tier 2	Suitable for Programmatic	3
Tier 3	Not Recommended	1

GWG Scores

App #	Title	Score	Median	SD	Low	High	Budget	Tier
SP3A-07536	Phase 1 Study of Genetically Modified Autologous Hematopoietic Stem Cells for HIV/AIDS	**76**	80	7	65	85	$5,583,438	**1**
SP3A-07552	Phase 1/2a Study of Allogeneic Oligodendrocyte Progenitors to treat Spinal Cord Injury	**76**	78	5	68	83	$14,323,318	**1**
SP3A-07526	Phase 2 study of a Small Molecule targeting CSCs for Triple-Negative Breast Cancer	**74**	72	10	60	90	$9,891,332	**2**
SP3A-07548	Phase 2b trial of Pharmacologically Modified Cord Blood for Transplantation in Patients with Hematological Malignancy	**71**	74	5	62	75	$9,496,582	**2**
SP3A-07559	Clinical Development of Bone Marrow Derived Progenitor Cells for Traumatic Brain Injury	**68**	70	8	55	85	$9,800,000	**2**
SP3A-07529	Phase 2 Study of Allogeneic Mesenchymal Bone Marrow Cellsfor Treatment of Acute Myocardial Infarction						$9,348,792	**3**

Programmatic Review

Tier 1

SP3A-07536: A Phase 1 Study in HIV -1 Infected Subjects to Assess Zinc Finger Nuclease CCR5 Modified Autologous Hematopoietic Stem Cells

Approach	Goal	Disease
Autologous Hematopoietic Stem Cells (HSC) genetically modified to disrupt CCR5	Phase 1 Trial	HIV/AIDS

- Project is a continuation of Disease Team I project
  - DTI end-goal is filing of IND
- Funds requested from CIRM: $ 5,583,438
- Applicant co-funding (required): $ 5,580,280

Tier 1

SP3A-07552: A Phase 1/2a Study of Allogeneic Oligodendrocyte Progenitors in Patients with Cervical Complete Spinal Cord Injury

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Approach	Goal	Disease
hESC-Derived Allogeneic Oligodendrocyte Progenitors	Phase 1/2a Trial	Spinal Cord Injury

- Funds requested from CIRM: $ 14,323,318
- Applicant co-funding (required): $ 19,638,687

Tier 2

Summary Staff Recommendations

App#	Disease Target	Approach	Staff Recommendation	Requested funding $M
SP3A-07526	Triple-negative Breast Cancer	Small Molecule targeting Cancer Stem Cells	**Do not fund**	$9.9
SP3A-07548	Blood Cancers requiring stem cell transplant	Ex vivo modification of Cord Blood Stem Cells	**Do not fund**	$9.5
SP3A-07559	Traumatic Brain Injury	Bone Marrow Derived Progenitor Cells	**Do not fund**	$9.8

Tier 2

SP3A-07526: Small Molecule targeting CSCs for Triple-Negative Breast Cancer

Deferred

Key Points Considered in Staff Recommendation

- **Triple negative breast cancer** (TNBC) is not susceptible to existing therapies for other subtypes of BC and is associated with worse outcomes i.e. there is an unmet medical need
- The therapeutic candidate targets the **CSC** associated with poor clinical outcome in TNBC and thought responsible for cancer progression and recurrence
- The proposed clinical trial is designed to directly test the "**cancer stem cell hypothesis**" which postulates that eliminating the CSC could cure the disease.
- The therapeutic candidate is a **small molecule** and is therefore likely to have access to alternative funding sources.
- CIRM recently awarded 3 **Disease Team III Awards** to fund early clinical trials for novel therapeutics aimed at targeting **CSCs**
- Weaknesses in the scientific merit of the proposal combined with portfolio considerations led to a **staff recommendation NOT to fund**

Deferred

Translation Portfolio: Cancer Stem Cells

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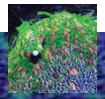
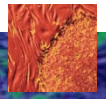
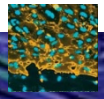
App #	RFA	Goal	Approach	Disease
DR3-07067 Slamon	DTIII	Phase 1 trial	Small Molecule inhibitor targeting CSC	Solid tumors
DR3-06965 Weissman	DTIII	Phase 1 trial	Antibody therapeutic targeting CSC	Solid tumors and acute myeloid leukemia (AML)
DR3-06924 Kipps	DTIII	Phase 1/2 trial	Antibody therapeutic targeting CSC	Chronic lymphocytic leukemia (CLL)
TR4-06867 Reiter	ET	Preclinical	Monoclonal antibody against N-cadherin positive CSC	Prostate cancer
TR2-01789 Jamieson	ET	Preclinical	Small molecule pan BCL-2 inhibitor targeting CSC	CML
TR2-01816 Müschen	ET	Preclinical	Small molecule inhibitor of BCL6 targeting CSC	AML, ALL

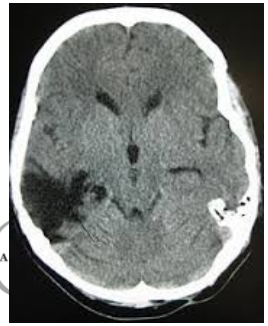
Tier 2

SP3A-07548: Phase 2b Trial of Modified Cord Blood for Transplantation in Patients with Hematological Malignancy

Key Points Considered in Staff Recommendation

- **Cord blood** has a number of advantages over other sources of hematopoietic stem cells (HSC) used for transplantation, but is hampered by delayed recovery
- The proposed project addresses a currently **unmet need** in the transplant field and the **scientific rationale** for the approach is compelling.
- Complete data from an ongoing Phase 1 study and a final FDA-approved protocol for the proposed Phase 2 study were not available at the time of the review. This was reflected in the overall score.
- There are **no other projects** in the CIRM portfolio aimed at overcoming barriers to the use of cord blood for hematopoietic stem cell transplantation.
- Although the scientific rationale and portfolio considerations are favorable, the absence of key Phase 1 data and a finalized protocol for the proposed clinical study led to a **staff recommendation NOT to fund**

Tier 2
SP3A-07559: Clinical Development of Bone Marrow Derived Progenitor Cells for Traumatic Brain Injury



Key Points Considered in Staff Recommendation

- The scientific rationale and supporting evidence to justify a clinical trial of the proposed approach in Traumatic Brain Injury are not strong.
- The proposed project is premature as key parameters such as the optimal timing to initiate treatment is still being evaluated.
- CIRM is funding an Early Translation project (TR2-01767) aimed at evaluating human embryonic stem cell-derived neural stem cells for use in Traumatic Brain Injury.
- Staff finds no compelling scientific or programmatic reason to recommend funding **/Do not fund**