CALIFORNIA'S STEM CELL AGENCY

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

The Duane Roth Disease Team Therapy Development III Awards: RFA 13-01 Grants Working Group Recommendations

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December 12, 2013

Agenda Item #15

RFA's Goals and Objectives

Purpose of the Disease Teams program is to advance preclinical and early clinical development of novel therapies

Two Objectives of this third call, the Duane Roth Disease Team Therapy Development III call for applications:

1) Complete an early phase clinical trial within the award period.
   - Proposed trial will evaluate preliminary safety and assess measures of preliminary biologic activity /efficacy in humans.
   - Up to 12-18 months of IND-enabling preclinical work allowed.

2) ONLY for CIRM Early Translational awardees who have successfully completed their ET project: objective is to file a well-supported IND (more info on this to come)

RFA Priorities

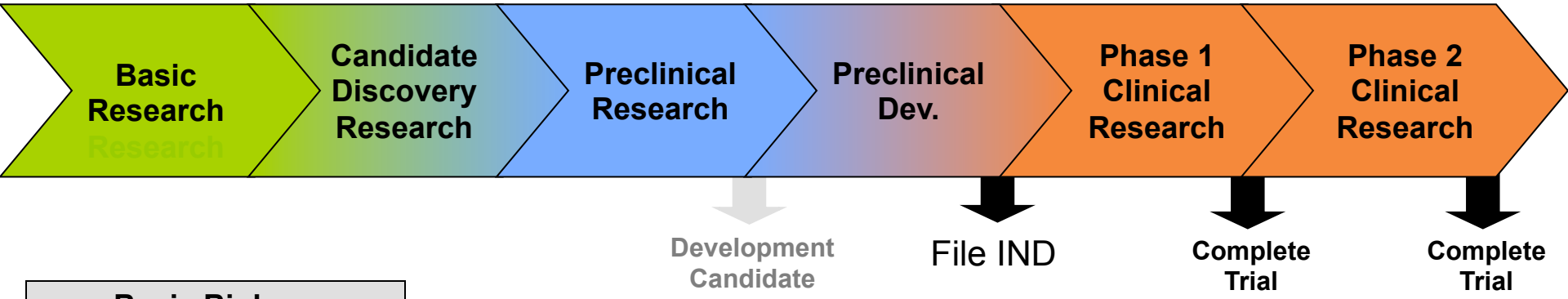
- Proposals that include a Phase 1 or Phase 2 clinical study that could demonstrate clinical proof-of-concept if successful.

- Proposals aimed at furthering the development of successfully completed CIRM-funded projects.

- Proposals that cannot, or are unlikely to, receive timely or sufficient federal funding.

Scope of Duane Roth Disease Team Therapy Development III

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



Basic Biology

Early Translational I,II, III, IV

Disease Team I

Disease Team Therapy Development II

Strategic Partnership I, II, III

Duane Roth Disease Team Therapy Development III

Note that Early Translational Allowance Pathway applications fit roughly here

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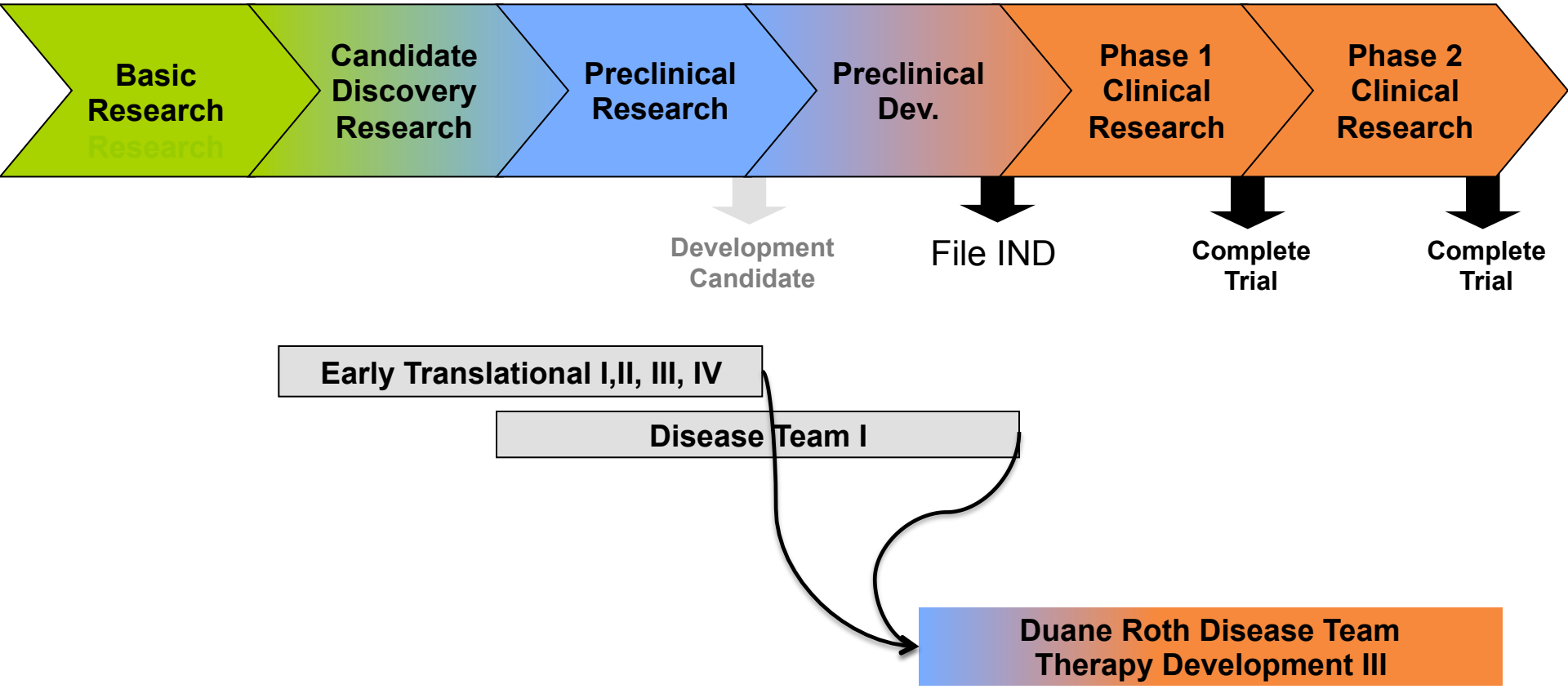

Eligibility Criteria

Eligibility criteria must have been met for the following:

- Eligible Therapeutic Candidate
- Institution
- PI
- Project Manager
- Co-PI (if applicable)
- Partner PI (if applicable)

GWG Expertise for DR3 Review

- Disease areas
- Product development
- Regulatory process
- Preclinical study design
  - (pharmacology/toxicology)
- Clinical trial operations
- Biostatistics

Review Criteria Used by GWG

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1. Significance and Impact
2. Scientific Rationale and Risk/Benefit
3. Therapeutic Development Readiness
4. Design and Feasibility
5. PI, Development Team and Leadership Plan
6. Budget
7. Collaborations, Assets, Resources and Environment
8. Intellectual Property and Licenses

Readiness for Clinical Trial Projects

- Proposing a Phase 2 study required Phase 1 safety data by May 15, 2013.

- Proposing a Phase 1 study required an IND filed with the FDA by March 13, 2013.

- Project on track for IND filing in 12-18 months must have held a pre-IND meeting with FDA by May 15, 2013 and
  - Single therapeutic development candidate selected.
  - Preclinical proof-of-concept shown in target disease/injury with the proposed therapeutic candidate.

Early Translational Allowance Pathway

- To ensure a pathway to success for current CIRM-funded projects, Early Translational (ET) awardees could apply with the goal of filing an IND within 4 years.

- Available ONLY to ET awardees who completed milestones and activities of the ET award to achieve a well-supported DC.

- 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 mechanism of action for regeneration and repair

Budget and Mechanism

- $5M to $20M per award over 4 years or less
- Up to $100M has been committed for up to 5 awards
- Awards to non-profit institutions will be in the form of grants.
  - For-profit institutions may choose a grant or a loan

Scientific Merit Scoring and GWG Recommendations

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

TIER 1 BUDGET	$42,752,978
TIER 2 BUDGET	$47,791,391

APP #	TITLE	SCORE	Median	SD	Low	High	BUDGET			
DR3-06924	Therapeutic Eradication of Cancer Stem Cells	79	80	4	70	85	$4,179,600	*	1	
DR3-06965	Clinical Investigation of a Humanized Anti-CD47 Antibody in Targeting Cancer Stem Cells in Hematologic Malignancies and Solid Tumors	79	80	5	70	85	$12,726,396	*	1	
DR3-07438	Phase 1 Safety Assessment of CPCB-RPE1, hESC-derived RPE Cell Coated Parylene Membrane Implants, in Patients with Advanced Dry Age Related Macular Degeneration	76	80	12	50	90	$18,922,665		1	
DR3-07067	A Phase I dose escalation and expansion clinical trial in patients with advanced solid tumors	76	78	5	65	80	$6,924,317		1	
DR3-07281	Tissue Engineered Recellularized Laryngotracheal Implants	70	70	7	60	78	$4,440,000	**	2	
DR3-07061	Subretinal delivery of human neural progenitor cells for the treatment of retinitis pigmentosa	69	71	8	50	80	$15,992,447		2	
DR3-06945	Clinical Trial of Stem Cell Gene Therapy for Sickle Cell Disease	69	70	4	64	80	$13,935,441		2	
DR3-07078	Embryonic Stem Cell-Derived Chondroprogenitor Cells to Repair Osteochondral Defects	67	70	7	50	75	$13,423,503		2	ET
DR3-06929	Allogeneic Glial Restricted Progenitor Cell Transplantation for Neuroprotection of Motor Neurons in Amyotrophic Lateral Sclerosis (Lou Gehrig's Disease)	63	68	18	20	85	$18,606,067		3	
DR3-07123	A Wnt-based therapy targeting endogenous stem cells to enhance skeletal healing in the elderly	-					$15,405,226		3	ET
DR3-07000	Harnessing Native Fat-Residing Stem Cells For Spine Fusion: From Early Translation To Disease Team	-					$18,861,314		3	ET
DR3-07307	Autologous Stem Cell Transplantation with Purified, anti HIV Gene Modified Stem Cells For Treatment of HIV Related Malignancies.	-					$10.982,932		3	
DR3-07201	DYNAMIC (Dilated cardiomYopathy iNtervention with Allogeneic Myocardlally-regenerative Cells) Trial: A randomized, double-blind, placebo-controlled Phase 1a/b multicenter study of allogeneic human cardiosphere-derived cells in patients with advanced heart failure	-					$12,895,092		3	

*Budget amount reflects allowable costs for in-scope activities.

**Budget amount reflects allowable amount for recommended preclinical activities.

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The Duane Roth Disease Team Therapy Development Awards III: Staff Recommendations

Bettina Steffen, MD

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Summary Staff Recommendations

App #	Disease Target	Approach	Staff Recommendation	$ (M)
DR3-07281	Tracheal transplant	Autologous stem/ progenitor cell plus scaffold	Fund with condition	$4.4**
DR3-07061	Retinitis Pigmentosa	Allogeneic neural progenitor cells	Do not fund	$16.0
DR3-06945	Sickle Cell Disease	Gene-modified autologous HSC	Fund	$13.9
DR3-07078	Osteochondral defects	Allogeneic hESC-derived chondrocyte progenitor plus scaffold	Fund	$13.4

**Budget amount reflects amount for recommended preclinical activities

DR3-07281: Tissue Engineered Recellularized Laryngotracheal Implants

- Focuses on developing tissue-engineered replacements for large airway disease
- Brings to California a novel technique and leverages more advanced work taking place in the UK
- Models technology transfer in a complex engineered product
- Creates opportunity to reproduce key preclinical data in an independent setting in a second, clinically relevant model
- The potential therapeutic would be tested and developed within California; and if the project advances into clinical development, early access would be available to citizens of California
- Fills gap in CIRM portfolio - hollow tube conduit tissue engineering approaches in the development portfolio; considered the logical entry point for 3-D replacement tissues

➢ **Staff Recommendation: Fund with condition**

DR3-07061: Subretinal delivery of hNPC for Retinitis Pigmentosa

- CIRM is funding two other Disease Teams and one Early Translational project aimed at retinal rescue or restoration. Different cell sources and target replacement cells are employed by the projects
  - One Disease Team (DR2A-05739) is developing a cell therapy in the same indication, Retinitis Pigmentosa
  - Another Disease Team (DR1-01444) uses a functionally polarized hESC-derived monolayer in Age-Related Macular Degeneration. A follow on project to conduct an early clinical trial is being presented today (DR3-07438) as Tier 1, Recommended for Funding
  - An Early Translational Award (TR4-06648) to develop hESC-derived "sheets" of retinal progenitor cells and retinal pigmented epithelial cells has recently been awarded

➢ **Staff Recommendation: Do not fund**

DR3-06945: Clinical Trial of Stem Cell Gene Therapy for Sickle Cell Disease

- Leverages the team and know-how gained in a Disease Team I project
- At most advanced development stage of the projects in the CIRM portfolio targeting blood diseases
- Sickle cell disease has a high unmet medical need
- Allows for a chance to detect evidence of biologic activity early in the trial in support of CIRM's strategic goal to demonstrate clinical proof-of-concept

➢ **Staff Recommendation: Fund**

DR3-07078: ESC-derived Chondroprogenitor Cells to Repair Osteochondral Defects

- Leverages the team and know-how gained in a completed Early Translation project
- At most advanced development stage of Early Translation projects in the CIRM portfolio targeting cartilage disorders and uniquely focuses on a pluripotent-derived progenitor cell
  - An Early Translational Development Candidate Feasibility Award (TR3-05709) to develop an autologous dermis isolated stem cell-derived tissue engineered product for the treatment of focal cartilage defects recently initiated.
  - An Early Translational Award (TR2-01829) is a small molecule to induce chondrocyte differentiation of resident MSCs for the treatment of osteoarthritis.
- Addresses CIRM portfolio gap - there are no funded Disease Team Awards or Strategic Partnership Awards in the CIRM portfolio in cartilage disorders

➢ **Staff Recommendation: Fund**