CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

The state stem cell agency

Disease Team Therapy Development Research Awards – RFA-10-05

Additional Analysis Results

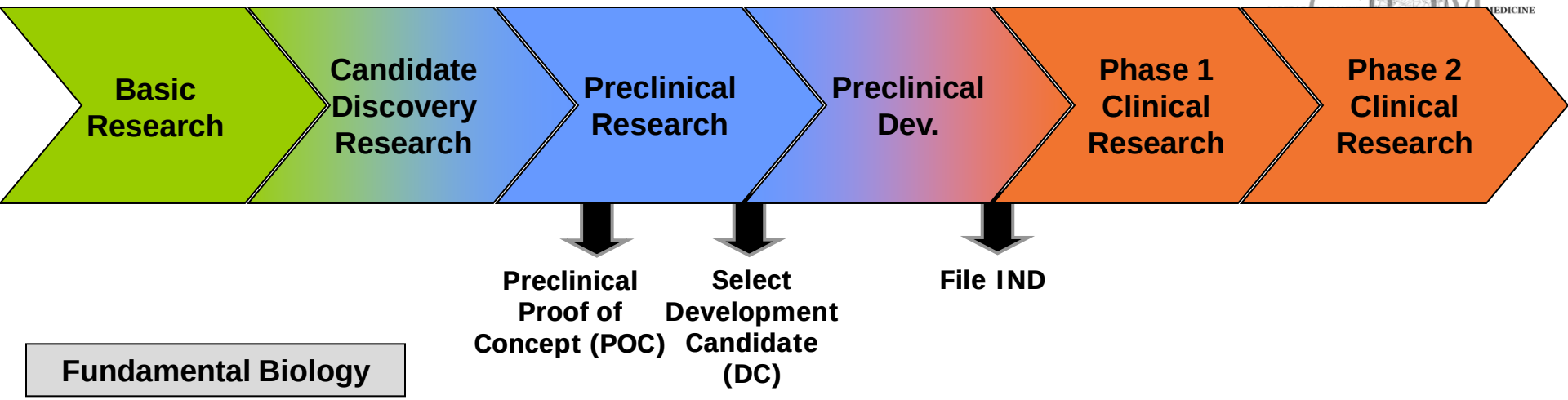
ICOC Meeting September 5, 2012
Agenda Item # 8

Providing context for the discussion…

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

- Briefly summarize RFA 10-05 Disease Team Therapy Development Research Award
- Recap of approvals from July 26, 2012 ICOC
- Description of additional analysis process
- Additional analysis results

Where does this RFA fit in CIRM's current portfolio programs



Fundamental Biology

Early Translational Research I,II, III

Disease Team Research I

Disease Team Therapy Development

Strategic Partnership I

Purpose is to advance preclinical and/or early clinical development of stem cell-based therapies

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Goal is to achieve, within the 4 year time frame

- Submit a well-supported IND for a clinical study
- Complete a Phase I or Phase I/II study
- Complete a Phase II study

Scope - must be cell-based, single therapeutic candidate

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

- Candidate derived from or utilizing hESCs, hiPSCs, neural stem cells, neural progenitor cells, or reprogrammed/genetically-modified stem cells
- Small molecule or biologic candidate characterized or generated using stem cells
- Candidate that targets cancer stem cells or endogenous stem cells in vivo
- Engineered functional tissue candidate for transplantation

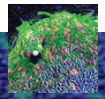
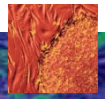
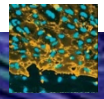
Review criteria

1. Significance and Impact
2. Project Rationale
3. Therapeutic Development Readiness
4. Feasibility of the Project Plan
5. Principal Investigator and Development Team
6. Collaborations, Resources and Environment
7. Conditions reviewed that were set at the time of the review of planning awards

GWG Expertise

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

- Preclinical studies including preclinical toxicology/safety
- Chemistry Manufacturing and Control (CMC)
- Disease/Clinical
- Regulatory
- Product Development

Recap of Recommendations and Decisions from July 26th ICOC

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

GWG recommendations

- 6 proposals recommended for funding, with budget up to $113M
  15 proposals not recommended for funding

ICOC deliberations

- ICOC asked CIRM Management scientific advice on 9 applications, and advised ICOC that 2 proposals deserved additional consideration - new data potentially addressing some key concerns in GWG recommendations

ICOC decisions

- Based on inputs from GWG, CIRM and public comment, ICOC voted to approve 8 proposals for funding, with budget up to $151 M
- Another 5 proposals sent for additional analysis

ICOC approved awards from July 2012

App DR2A #	Score	Disease Area	Approach	Goal
05415	87	Huntington's Dis	Allogeneic gene-modif MSC	Ph 1/2 trial
05309	84	Melanoma	Autologous gene-modif MSC	Ph 1 trial
05302	80	Osteoporosis	Small molec	Ph 1 trial
05423	79	Critical Limb Ischemia	Allogeneic gene-modif MSC	Ph 1 trial
05736	79	Cerv. Sp. Cord Injury	Allogeneic hNSC	IND
05394	68	End Stage Heart Failure	Allog hESC deriv cardiomyocytes	IND
05320	64*	ALS	Gene-modif fetal derived NSC	Ph 1 trial
05365	53*	SCID	Monoclonal Ab	Ph 1 trial

*Moved to funding level
Budget up to total $151 M

July 2012 ICOC referred proposals for additional analysis

App DR2A #	Score	Disease Area	Approach	Goal	Budget $ in M
05416	61	Alzheimer's Dis	Fetal derived NSC	IND	20.0
05739		Retinitis Pigmentosa	Allogeneic hRPCs	Ph 1/2 trial	17.3
05426		Duchenne Muscular Dystrophy	Antisense oligonucleotide and small molecule	IND	20.0
05352		Breast cancer	Monoclonal Ab	Ph 1/2	20.0
05735		Post MI heart failure	Allog cardiac derived stem cells	Ph 2 trial	19.8

The additional analysis process

- ICOC directed President, Co-Vice Chair of GWG to establish the process, in consultation with the Chair, ICOC and CIRM scientific staff
- Additional analysis conducted by:
  - Review Chair, GWG
  - Another scientific member, GWG (selected based on expertise necessary to assess the new information)
  - Patient advocate, GWG
- Charged to evaluate specific new information, available after GWG review, and determine whether information addressed reviewers' key concerns and would have impacted overall recommendation by GWG for funding

The additional analysis process

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

- For each of 5 applications, reviewers had access to the following:
  - New material (see pre-read for list)
  - Original application
  - Review critique
  - Petition
- Each application assessed independently, and telecon to discuss each one
- Provide results at the September ICOC

Additional analysis results

App DR2A #	Disease Area	Approach	Goal	Budget $ in M	Addit. Analysis results
05416	Alzheimer's Disease	Fetal derived NSC	IND	20.0	No change in GWG -NR
05739	Retinitis Pigmentosa	Allogeneic hRPCs	Ph 1/2 trial	17.3	Change in GWG -Recomm
05426	Duchenne Muscular Dystrophy	Antisense oligonucleotide and small molecule	IND	20.0	Modified GWG – Recomm for ET
05352	Breast cancer	Monoclonal Ab	Ph 1/2	20.0	No change in GWG - NR
05735	Post MI heart failure	Allog cardiac derived stem cells	Ph 2 trial	19.8	Change in GWG – Recomm with conditions

Back-up slides

DR2-05415 – MSC engineered to produce BDNF for the treatment of Huntington's disease

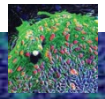
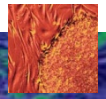
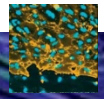
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
Allogeneic mesenchymal stem cells (MSC) genetically engineered to secrete brain-derived neurotrophic factor (BDNF) to treat Huntington's disease	IND, observational clinical trial and Phase 1 clinical trial	Huntington's disease

DR2-05309 – Genetic Re-programming of Stem Cells to Fight Cancer

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
Autologous Hematopoietic Stem Cells (HSC) genetically engineered to redirect patient's immune response against advanced form of the aggressive skin cancer	IND and Phase 1 clinical trial	Melanoma

DR2-05302 – Treatment of Osteoporosis with Endogenous Mesenchymal Stem Cells

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
A small molecule, LLP2A-Ale that directs endogenous mesenchymal stem cells (MSCs), to the bone surface to form new bone	IND and Phase 1 clinical trial	Osteoporosis

DR2-05423 – Phase I Study of IM Injection of VEGF-Producing MSC for the Treatment of Critical Limb Ischemia

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
Allogeneic mesenchymal stem cells (MSC) genetically engineered to produce vascular endothelial growth factor (VEGF) and promote blood vessel growth	IND and Phase 1 study	Critical Limb Ischemia

DR2-05736 – Neural stem cell transplantation for chronic cervical spinal cord injury

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
Allogeneic neural stem cell transplantation to treat chronic cervical spinal cord injury	IND	Spinal Cord Injury (cervical)

DR2-05394 – Human Embryonic Stem Cell-Derived Cardiomyocytes for Patients with End Stage Heart Failure

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
Allogeneic hESC-derived cardiomyocytes to treat end stage heart failure	IND	Heart failure

DR2-05320 – Progenitor Cells secreting GDNF for the Treatment of ALS

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
Gene modified fetal derived NSC	Phase 1	Amyotrophic Lateral Sclerosis

DR2-05365 – A Monoclonal Antibody that depletes Blood Stem Cells and Enables Chemotherapy Free Transplants

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
Monoclonal antibody targeting CD117 on blood forming stem cells	Phase 1	Severe Combined Immunodeficiency

DR2-05739 – Retinal Progenitor Cells for Treatment of Retinitis Pigmentosa

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
Allogeneic hRPCS	Phase 1/2	Retinitis Pigmentosa

DR2-05735 – Allogeneic Cardiac-Derived Stem Cells for Patients Following a Myocardial Infarction

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
Allogeneic heart stem cells	Phase 2	Heart attack

DR2-05426 - Combination Therapy to Enhance Antisense Mediated Exon Skipping for Duchenne Muscular Dystrophy

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Approach	Goal	Disease
Antisense oligonucleotide and small molecule	IND	Duchenne Muscular Dystrophy