CALIFORNIA'S STEM CELL AGENCY

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Advancing Stem Cell Science– CIRM's Scientific Scope and Programs

Ellen G. Feigal, M.D.
Senior Vice President, Research and Development

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CIRM's Vision and Strategy

Mission

"To support and advance stem cell research and regenerative medicine under the highest ethical and medical standards for the discovery and development of cures, therapies, diagnostics, and research technologies to relieve human suffering from chronic disease and injury"

Explore (2004-2010)

- Fund broad number of diseases and projects
- Establish foundation for leadership in stem cell research

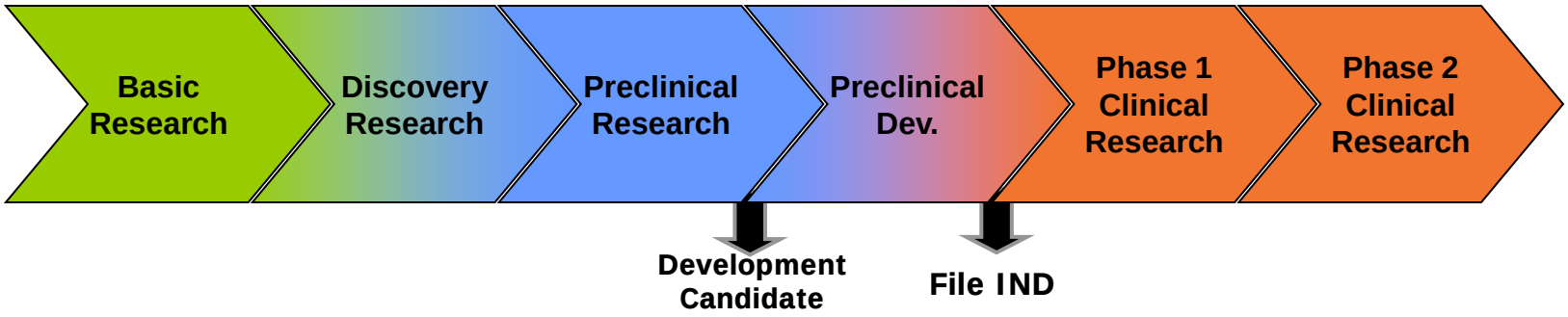
Focus (2011-2016)

- Prioritize projects and investments
- Drive clinical trials for patients to generate preliminary evidence of therapeutic benefit
- Develop partnerships

Deliver (2016+)

- Facilitate commercialization of therapies
- Advance therapies to patients
- Enable business model for stem cell-based therapies

Where have the $ been invested? CIRM's research funding commitment



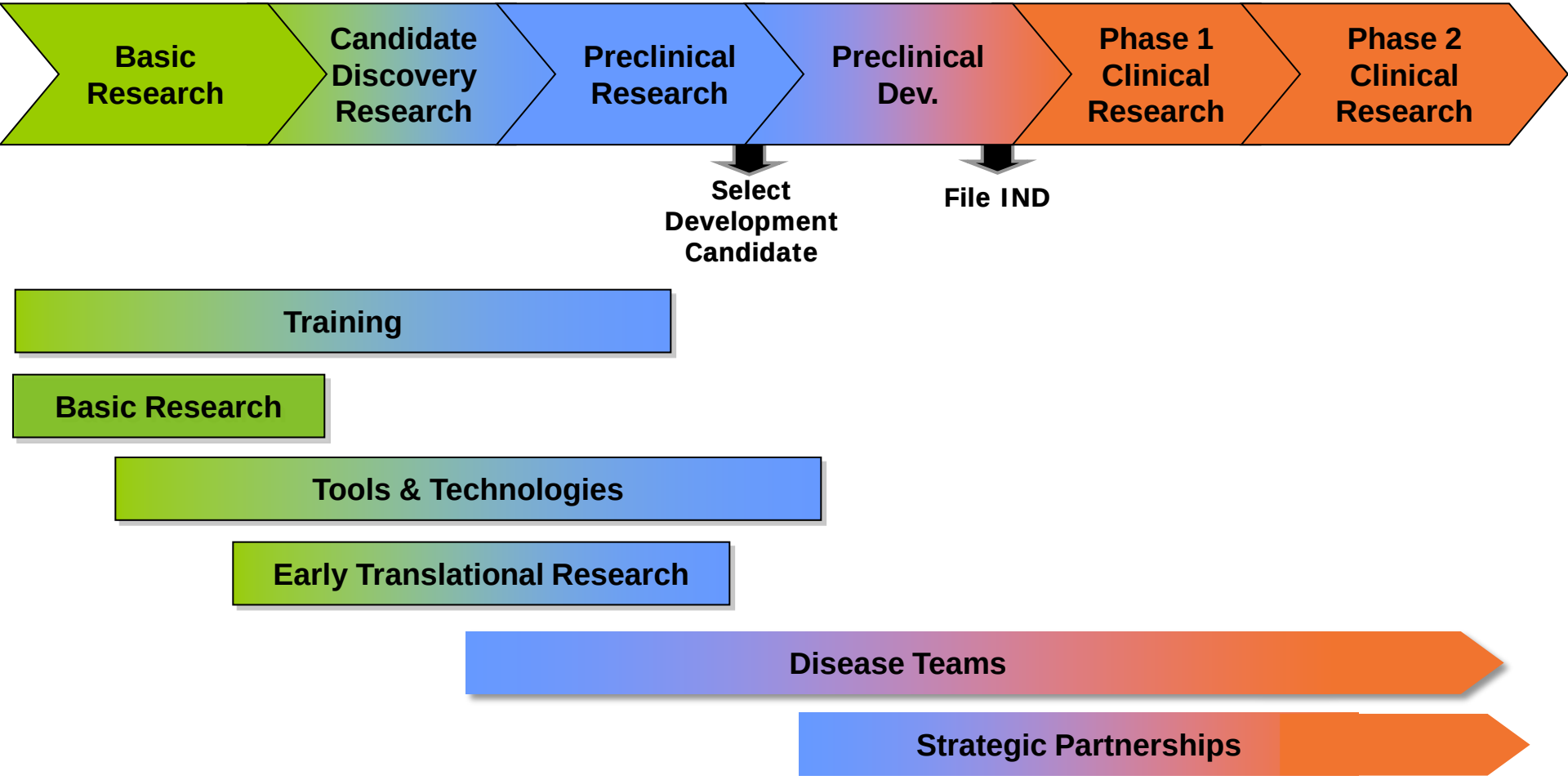
Infrastructure: Facilities & Cores - $374.3 MM

Infrastructure: Intellectual - $403.0 MM

Pipeline: Foundational Research - $387.3 MM

Pipeline: Translational Research - $790.1 MM

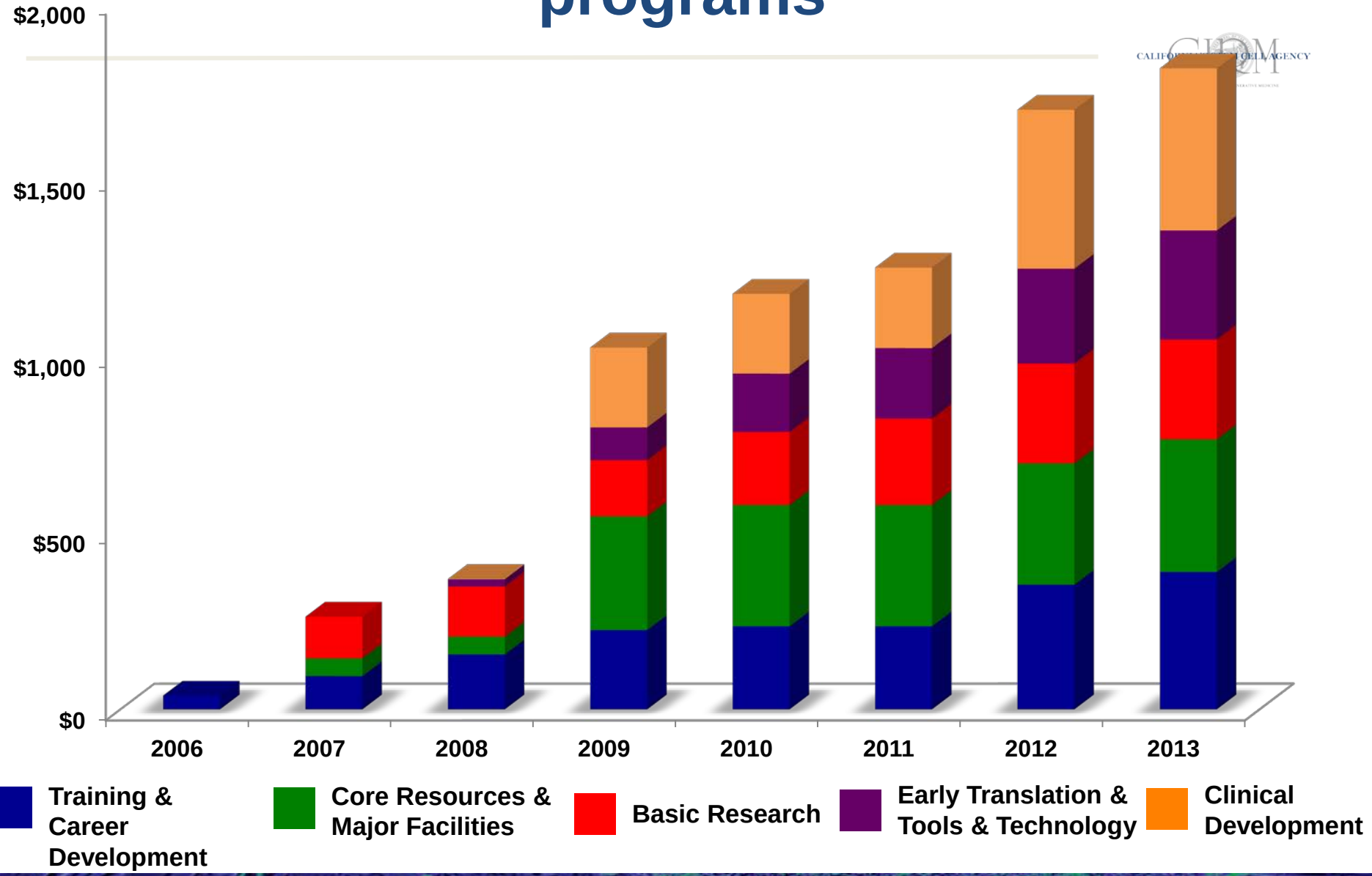
CIRM's core programs provide a pathway spanning scientific advances to therapies



CIRM activities toward our mission

- Approx 600 awards > 60 institutions and organizations for training, basic, tools n tech, translation/development
- Hundreds of collaborations between academic researchers, across state, US, and internationally
- Co-funding with 21 countries,states,foundations,NIH
- Productive interactions with regulatory agencies, alliance for regenerative medicine, prof societies
- More than 80 programs moving towards or in clinic; collaborations, leverage expertise and $ with companies
- 25 development teams: 7 collaborative funding partners; 1 collaboration with disease foundation; 7 have companies as PI/co-PI; 3 founded companies; 2 licensing partnerships with large biopharma

Cumulative ICOC approved funding in core programs



Breakdown: CIRM Training & Bridges Program Initiatives

RFA (Year Approved by ICOC)	# of Awards	Funds Approved by ICOC (MM)
Training	33	$130.9
Training I (2005)	16	$38.9
Training II (2008)	17	$45.2
Training Extensions (2011)	17 (from Training II)	$46.8
Bridges	16	$50.6
Bridges I (2008)	16	$24.0
Bridges Extensions (2011)	16 (from Bridges I)	$26.6
Totals	**49**	**$181.5**

CIRM Training & Bridges Programs

Training: Predoctoral candidates , post doctoral and clinical fellows

- Mentored laboratory stem cell research
- Course work: Stem cell biology – application to health and disease; ethical legal and social aspects of stem cell research
- To date: 751 CIRM Scholars at 17 institutions, 400 labs
- Survey 2013: 37% of 430 scholars in advanced training or another degree; 56% positions as academic research faculty, in biotech or pharma, or in teaching, medical practice, or foundation/govt work

Bridges: Undergraduate, Master's degree candidates especially from CSU and community colleges

- Over 500 mentored internships stem cell research in 46 institutions, over 300 laboratories in research-intensive universities and biotech companies

Plan competitive round of training & bridges

Training Program: CIRM Scholar

Joyce Lee,

- Clinical fellow in CIRM UC Davis Stem Cell Training Program
- Completed pharmacy practice and oncology pharmacy specialty residencies
- Research in neuroblastoma - the most common extracranial solid tumor occurring in children - working on developing more effective, less toxic treatments
- Received Hyundai Hope on Wheels **Pediatric Cancer Research Young Scholar Award** as a result of her work that was supported by the CIRM UC Davis Stem Cell Training Program

Current Position: Assistant Professor in the Division of Hematology/Oncology, Department of Internal Medicine, UC Davis

CIRM Bridges Program Intern

Sarah George

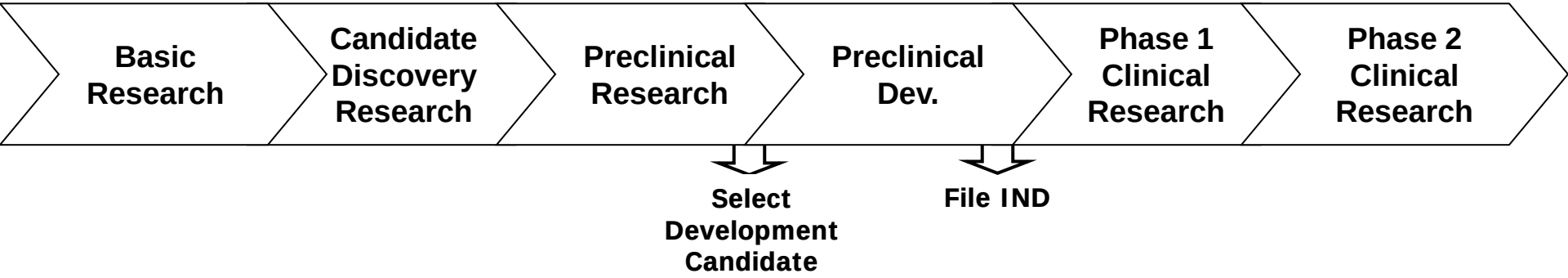
- CSPU San Luis Obispo Bridges Program
- Bridges internship at UC San Diego in lab of Dr. Karl Willert, Dept, of Cellular and Molecular Medicine.
- Completed Masters degree in Biomedical Engineering

- Current Position: research associate at NeuroGeneration working on the development and application of neural stem cells for therapeutic use in treating neurodegenerative disease

Breakdown: CIRM Basic Research Initiative

RFA (Year Awarded by ICOC)	# of Awards	ICOC Approved Funding (MM)
SEED (2007)	73	$45.3
Comprehensive (2007)	28	$72.0
Basic Biology	110	$154.5
Basic Biology I (2009)	12	$16.3
Basic Biology II (2010)	16	$22.4
Basic Biology III (2011)	27	$37.8
Basic Biology IV (2012)	25	$38.0
Basic Biology V (2013) *	30	$40.0
Totals	**211**	**$271.8**

Basic Research Program

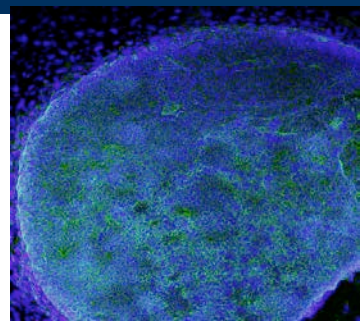


SEED Awards

Comprehensive Awards

Basic Biology I, II,III, IV, V

Basic Research Program Focus: Human Stem Cells



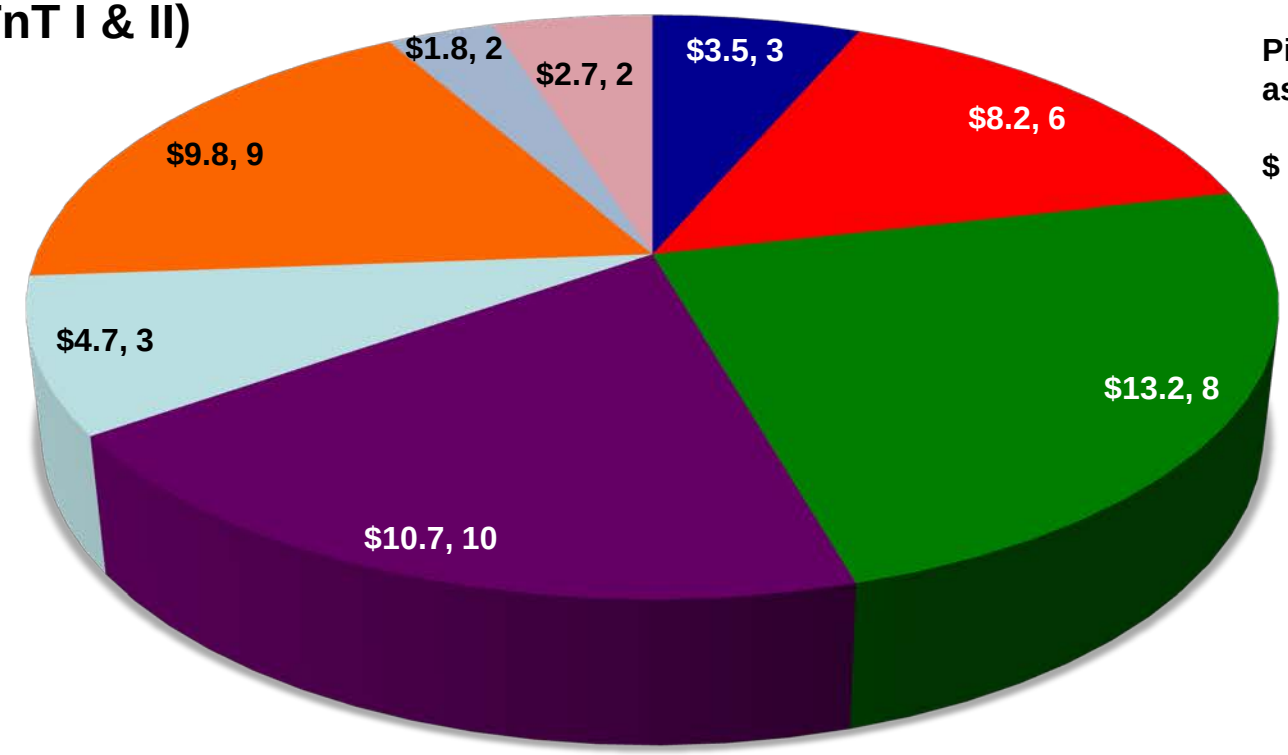
- Supports basic research on **human** stem/progenitor cells
  - 211 Principal Investigators
- Attract researchers new to human stem cell research: SEED program:
  - Attract investigators new to embryonic stem cell research into the field to conduct research on the biology, derivation and application of hESC and their derivatives
  - 31/72 (42%) SEED investigators received 38 other CIRM research grant(s)
- Plan 2 more rounds of basic biology

Breakdown: CIRM Tools & Technology Initiative

RFA (Year Approved by ICOC)	# of Awards	ICOC Approved Funds (MM)
Tools & Technology I (2008)	23	$19.8
Tools & Technology II (2011)	20	$34.7
Tools & Technology III (2014) *	20	$35.0
Total	63	$89.5

Breakdown: CIRM Tools & Technology Initiative

43 Awards (TnT I & II) comprise $54.5 M
TnT III now 63 awards $89.5M



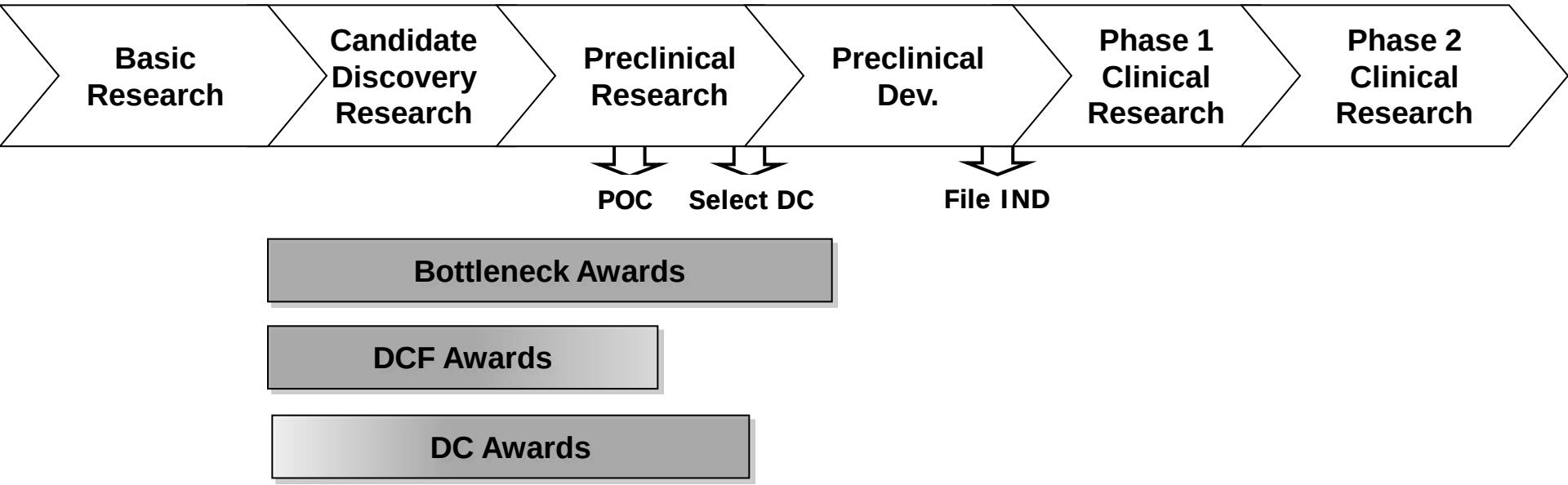
Pie slices are labeled as follows:

$ M, # of Programs

Breakdown: CIRM Early Translation Initiative

RFA	Program Period	Grants Awarded, #				Funds Committed, MM			
		B*	DCF	DC	Total	B*	DCF	DC	Total
ET I	2009 - 2013	7	---	9	16	$29.5	---	$43.9	$73.4
ET II	2011 - 2014	---	9	12	21	---	$16.7	$54.7	$71.4
ET III	2012 - 2015	---	11	10	21	---	$19.6	$49.8	$69.4
ET IV	2013-2016	---	8	5	13	---	$15.4	$25.3	$40.7
TOTAL		**7**	**28**	**36**	**71**	**$29.5**	**$51.7**	**$173.7**	**$254.9**

Early Translation Awards

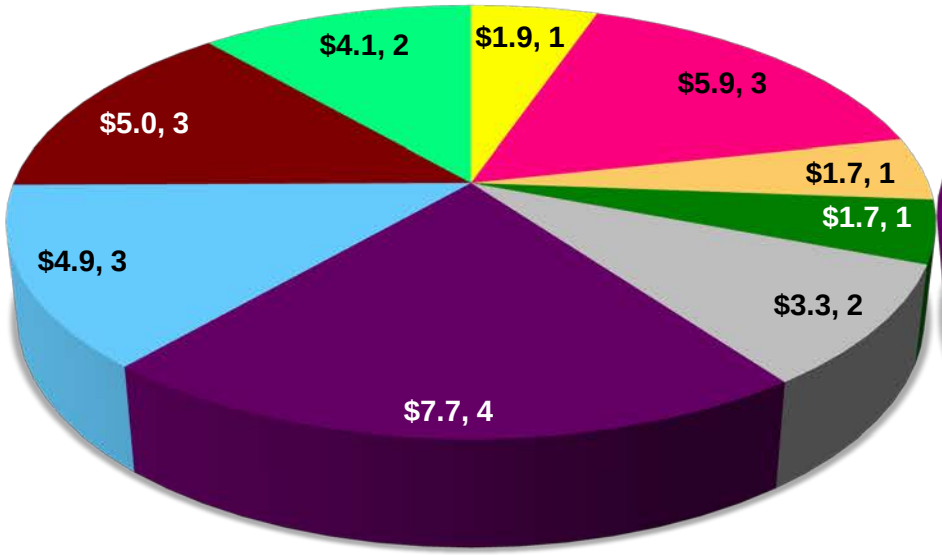


CIRM Early Translation Program

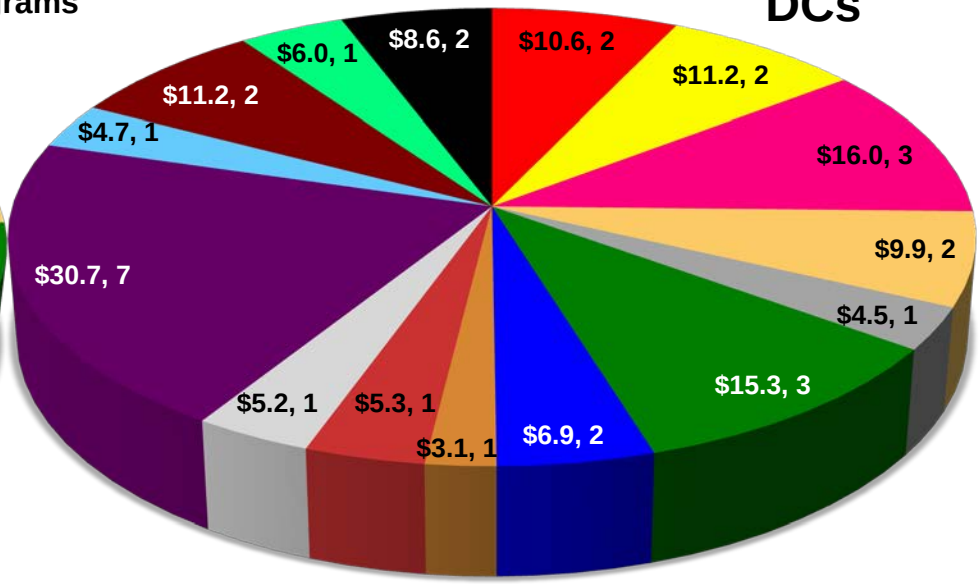
ET I-III 51 Early Translation Programs, funding commitment of $185.4 MM; latest round ETIV total is 64 awards $225.4M

Pie slices are labeled as follows:
$ MM, # of Programs

DCFs



DCs



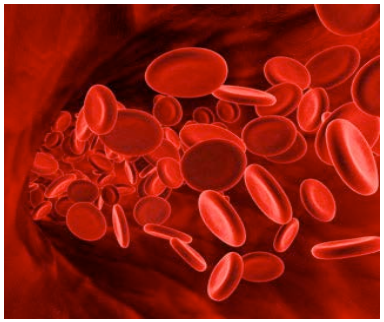
- Blood Disorders
- Bone Disorders
- Cardiovascular Disorders
- Cartilage Disorders
- Endocrine Disorders
- Eye Disorders
- Hematologic Cancers
- HIV/AIDS
- Kidney/Urinary Disorders
- Liver Disorder
- Neurodegenerative Disorders
- Neurologic Injuries
- Pediatric Neurological Disorders
- Skeletal Muscle Disorders
- Solid Cancers

Early Translation Research Outcomes
Early Translation ➡ Disease Team

TR2-01272 ➡ DR2A-05739

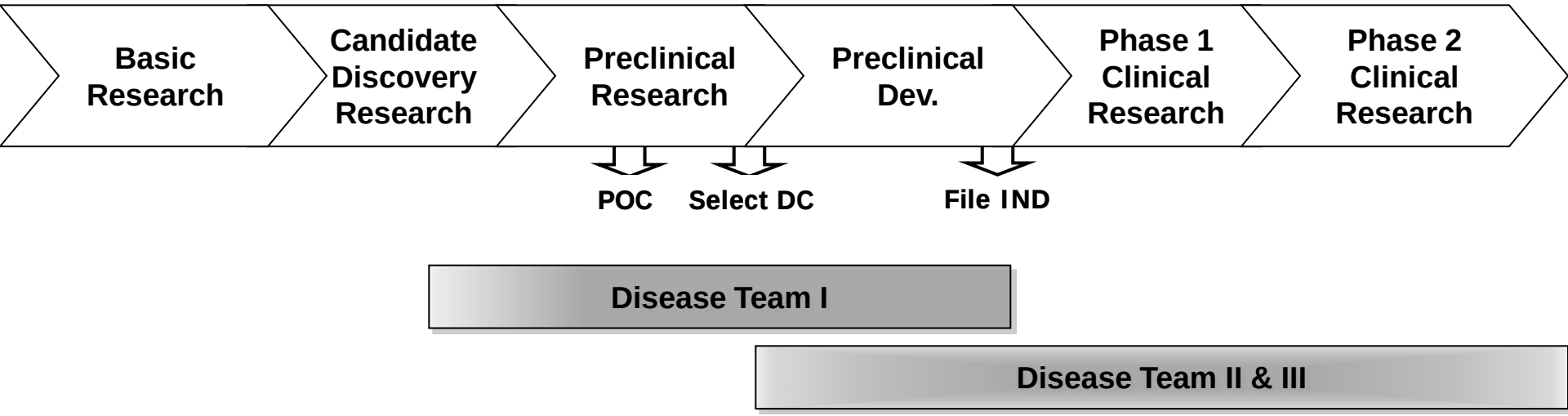
- Klassen, UCI
- Disease: Retinitis Pigmentosa
- Approach: Allogeneic retinal progenitor cells

Early Translation I, II Research Awards: Blood Disorders



- TR1-01272, Verma, Salk Institute
  - Goal is to take the patient's own pluripotent stem cell -derived blood stem cells and correct the genetic defect to treat patients with the severe blood disorders of Fanconi Anemia, and X-linked severe combined immunodeficiency (X-SCID)
  - Derived pluripotent stem cell (iPSC) lines from skin samples from patients, and generated preclinical mouse models of these severe blood disorders
  - Developed and demonstrated a robust and reproducible method for an efficient way to generate multipotent blood progenitor cells from embryonic stem cells and from iPSC, and found that in short term studies these cells could engraft (published).
- Plan 2 more rounds of ET awards

Disease Team Research Awards

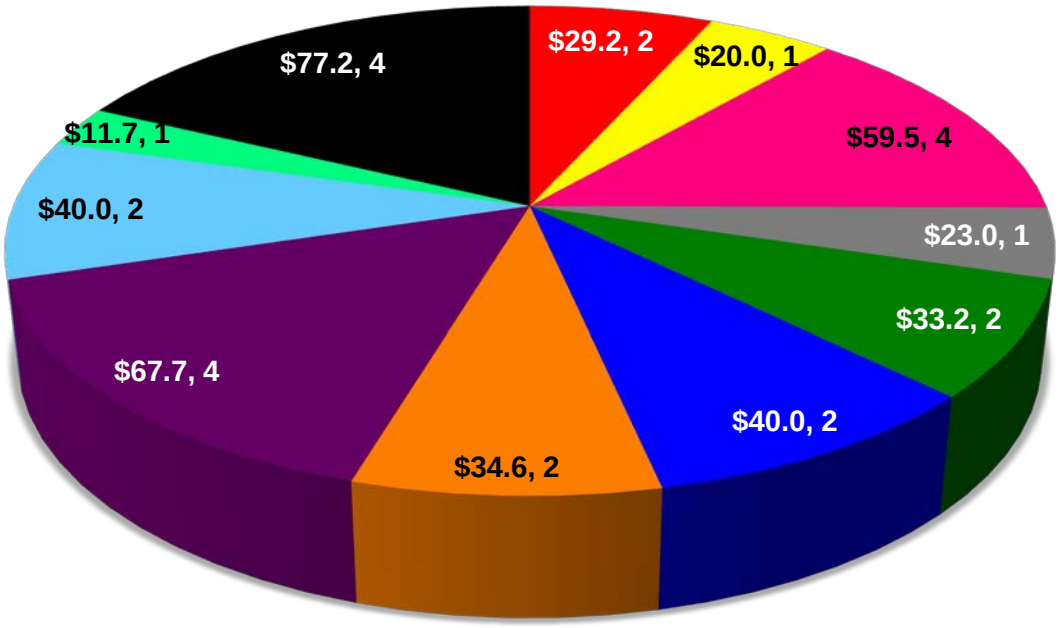


CIRM Development (Disease Teams and Strategic Partnerships): Target End Goals

RFA (Year Awarded by ICOC)	# of INDs	$ (MM) towards IND	# of Early Stage Clinical Trials	$ (MM) towards Early Stage Clinical Trials
Disease Team I (2009)	14	$228.0	0	$0
Disease Team II (2012)	3	$60.0	8	$148.1
Disease Team III (2013)	1	$4.4	5	$56.7
TOTALS	**18**	**$292.4**	**13**	**$204.8**
Strategic Partnership I, II			2	$16.4

CIRM Development Teams Initiative

Disease Teams I, II
$436.1 M;
with DT III, SP I, II
$513.6M



Pie slices are labeled as follows:

$ M, # of Programs

Blood Disorders
Bone Disorders
Cardiovascular Disorders
Endocrine Disorders
Eye Disorders
Hematologic Cancers
HIV/AIDS
Neurodegenerative Disorders
Skin Disorder
Neurologic Injuries
Solid Cancers

Example: Development Team project headed into clinic: Targeting key lesion in age-related degenerative eye disease – retinal pigment epithelium

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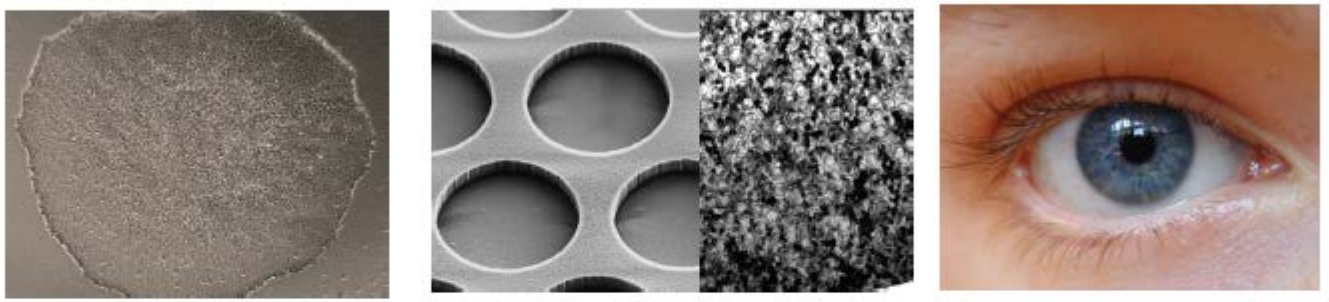
The Regenerative Implant:

Therapy for Dry Age-Related Macular Degeneration



Regenerative Patch Technologies™

Example:Development Team project headed into the clinic: Targeting lesion in diabetes – glucose sensing insulin production

VC-01™ Combination Product – Improving Diabetes Treatment

ViaCyte has integrated two of its novel technologies, PEC-01™ cells and the Encaptra® drug delivery system, into one therapy called VC-01™ combination product.

Example: Development Team projects headed into clinic: Targeting Entry Point for HIV

- 2 approaches (Calimmune, and City of Hope/Sangamo) for Hematopoietic Stem/Progenitor Cell Based Therapy for HIV Disease
  - To provide a one-time/infrequent outpatient treatment that will reduce (if not eliminate) the requirement of HAART for HIV+ patients.
- Calimmune project is in the clinic, enrolling patients

In addition to funding, CIRM helps teams build product development experience

Programs driven by science and evidence, and regulatory considerations needed on development pathway


AP / Damian Dovarganes

- Prior to award
  - Go, no go, progress milestones, and success criteria
- During research
  - review preclinical/clinical protocols, regulatory strategy, prep for interactions with FDA, attend team meetings
- Education and training of teams through CIRM/FDA webinars, roundtables, conferences, seminars

CIRM works with FDA and other agencies on regulatory pathways for cell therapy

International Regulatory Workshop: Pathways for Cell Therapies CIRM-led workshop Sept 2013;
N. American, European, and Japanese regulatory frameworks for developing cell-based therapies

CIRM webinars, roundtables and workshops topics:

cell characterization, preclinical animal studies, imaging technology, immune response, scaffolding, clinical trials
http://www.cirm.ca.gov/our-funding/regenerative-medicine-consortium

CIRM works with external Advisors on development projects at key milestones

- Clinical Development Advisory Panel (CDAP) complements CIRM's interactions with development teams
  - Experts in product development, e.g., preclinical and clinical, cell process and manufacturing, regulatory, stem cell/disease-specific biology, disease-specific clinical expertise and commercial relevance
- Yearly meetings with each Development team to assess key milestones
- Advice helps informs CIRM decisions
  - Continue forward progress; refine approach e.g., modify milestones, timelines, budgets; convert the project to an earlier phase with reduced scope and budget, or terminate the project

Capricor and Janssen Enter Collaboration for heart disease

- Capricor was awarded a CIRM Disease Team II of $20 million for the completion of a Phase 2 clinical trial for patients who have heart failure after a large heart attack
- Collaboration with Janssen for CAP-1002 (allogeneic adult stem cell therapy) in heart failure

Sangamo BioSciences Collaboration with Biogen Idec for Blood Diseases

- Sangamo was awarded $6.4 million under CIRM's Strategic Partnership Award, and 1-1 required matching funds
- Collaboration with Biogen Idec for Beta-Thalassemia and Sickle Cell Disease

Summary of Development Team highlights

- >50% of development teams have successfully advanced through their milestone meeting with FDA, towards an approvable IND to enter clinical trials in patients
- 3 INDs filed, 2 clinical trials started 2013 – 1 in patients with HIV, and 1 in patients with heart failure after a heart attack
- Expect 6 IND filings and 5 to 6 clinical trials by end of 2014
- 7 collaborative funding partners; 1 collaboration with disease foundation; 7 have companies as PI/co-PI; 3 founded companies; 2 collaborative partnerships with large biopharma for follow-on financing

Summary of Development Team highlights

- Plans for Development include:
  - Accelerated pathway; concept approved by ICOC in Dec 2013 with set-aside of $200M
  - Additional rounds of Development Teams
  - Enhanced interactions with commercial entities

Prioritization – what is it?

Identify 6 to 8 development projects (from currently funded disease teams or strategic partnerships, while still allowing a porous window for new mature projects to competitively enter) that have the potential to reach clinical proof of concept in/by 2017, consistent with CIRM's Strategic Plan, and facilitate their movement through CIRM's "Accelerated Pathway"

Recommended by CIRM's external Scientific Advisory Board in October 2013, and CIRM concept approved by ICOC in December 2013

Accelerated Pathway – what is it?

- Accelerated pathway
  - More frequent and extensive discussions with Clinical Development Advisors and CIRM scientific staff on preclinical, manufacturing, regulatory, clinical, and commercial aspects of developing the therapy
  - Finance essential development components as they arise, and as needed, follow-on phase 2 trials.
  - Projects will be selected from already GWG recommended and ICOC funded solicitations (disease teams and strategic partnerships), and will already have CIRM funding for early phase clinical trials

Clinical Proof of Concept – value to patients, the public, and to investors

Scientific Advisory Board recommendation directly aligns with clinical goal of CIRM's Strategic Plan, to advance stem cell science towards evidence of safety and activity in patients e.g., clinical proof of concept

Clinical Proof Of Concept

- Tangible endpoint that has meaning for patients and the public who brought CIRM into existence
- Important inflection point for attracting investors and moving towards commercialization

Options to consider for criteria – what does CIRM really want? Make it clear

- Stem cell therapies where the stem cell connection is strong and compelling
- Clear and strong plan for the development pathway
- Potential for major impact is strong
- Diseases with an accepted or reasonable marker of activity relevant to the disease, some (preferably good) understanding of the mechanism and pathophysiology of the disease, and what it takes to establish efficacy, such that clinical trials with well-defined, biologically quantifiable endpoints can be planned, and primary clinical endpoint is clear and well established
- Proof of concept possible in/by 2017
- Strong, credible team with expertise in development and ability to execute on plans

Budget

- $200M for follow-on phase 2 trials, where required and appropriate to achieve clinical proof of concept, for up to 6 to 8 projects
  - Funding would be set-aside from already designated funds for Development