CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

The state stem cell agency

CIRM Translational Portfolio Status Update

Patricia Olson, Ph.D.
Executive Director, Scientific Activities

Ellen Feigal, M.D.
Vice President, Research & Development

Agenda Item #6

Objectives

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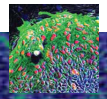
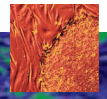
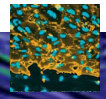
- Provide ICOC/Board an informational overview of our current translational portfolio
- Serve as the basis for ongoing discussions with the ICOC/Board on, for example portfolio project progress, therapeutic area distribution, and investment
- Provide a reference and a context for ICOC/ Board decisions
  - For example, balance of new projects and follow-on funding to existing promising, performing and competitive projects

Current Portfolio Programs

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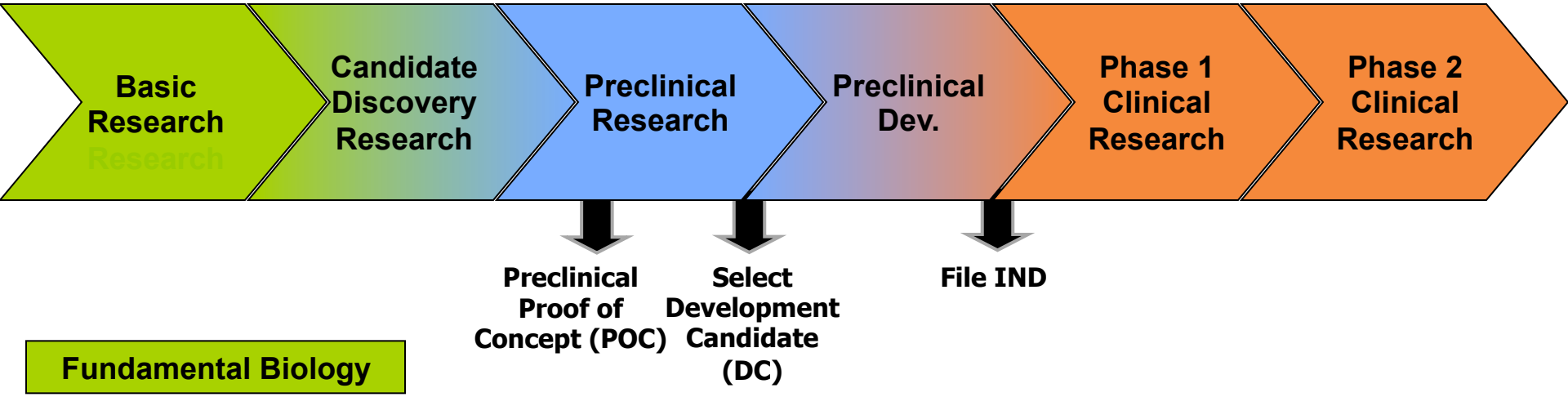

Fundamental Biology

Early Translational Research I,II

Disease Team Research I

Targeted Clinical Development

Disease Team Research II

Translational Portfolio, Current

CIRM's Collaborative Funding Partners: Leveraging Expertise and Resources

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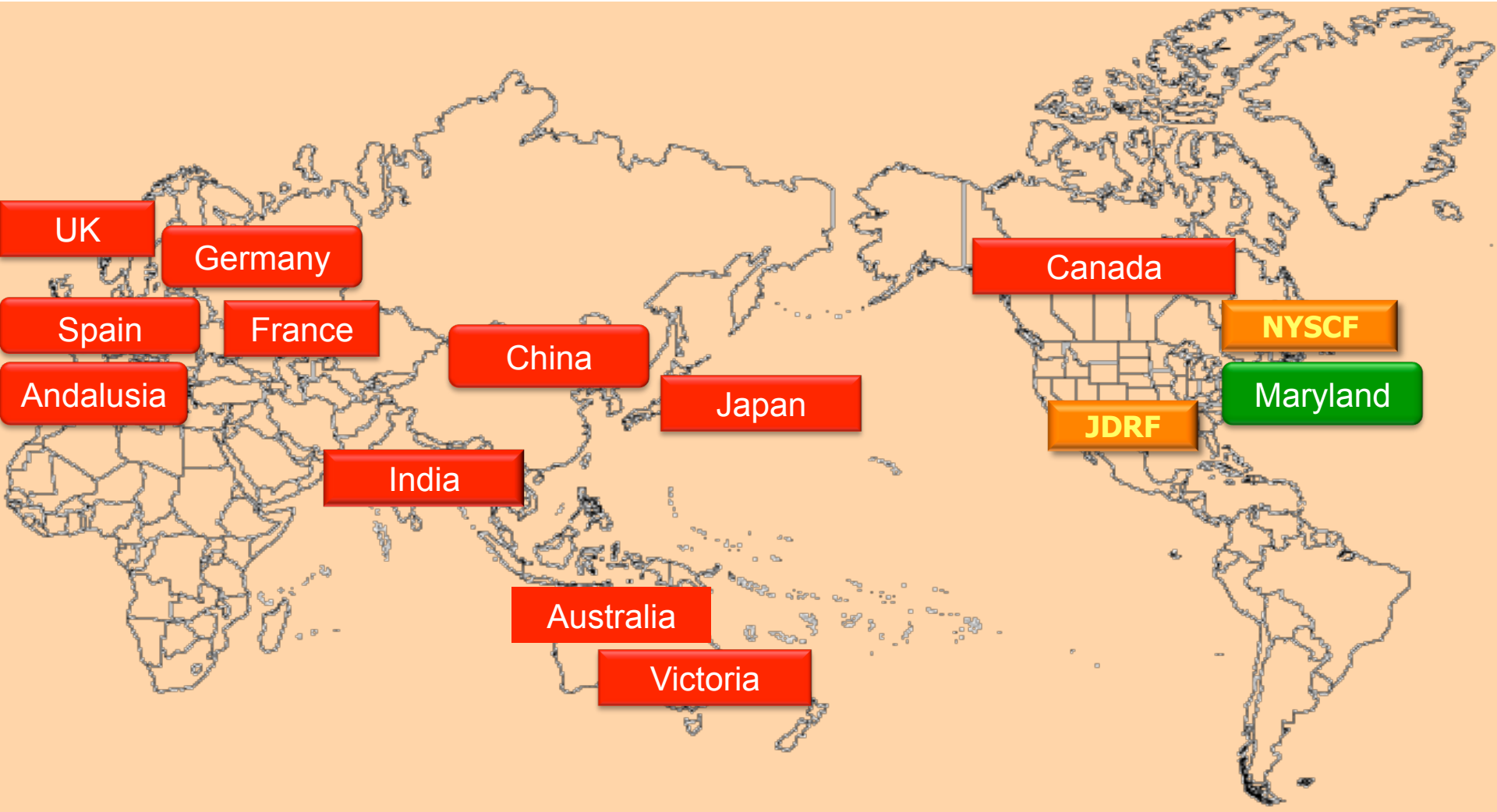

Translational Portfolio: Cumulative Growth

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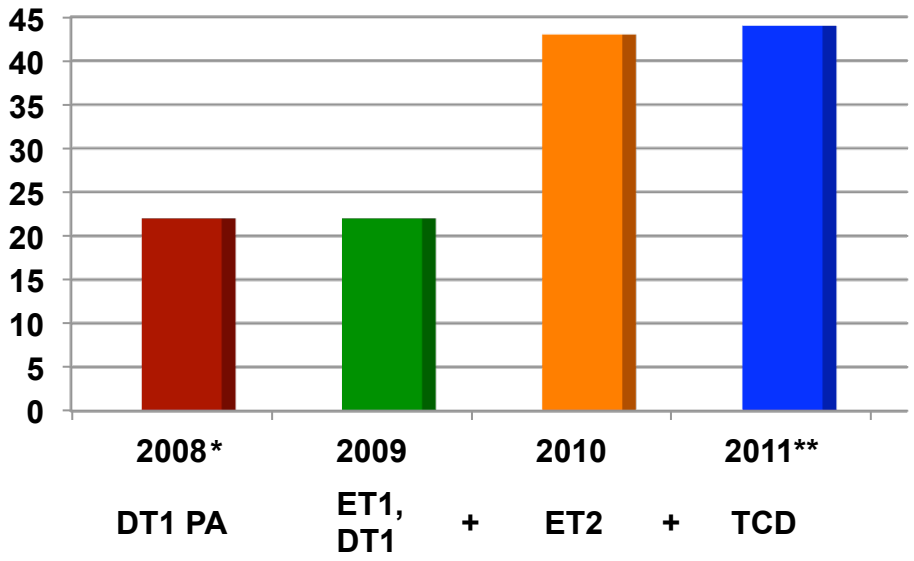
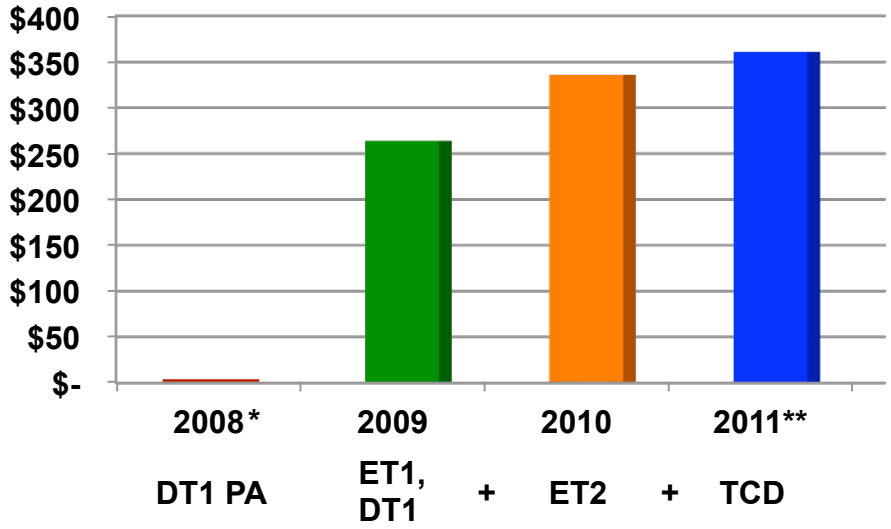
ICOC Approved Awards,



ICOC Awarded Funds, $ MM



	2008	2009	2010	2011 **
# Grants	22	22	43	44
Money Awarded (in MM)	$1	$264	$336	$361

* Closed Out

** Year to date

Translational Portfolio: Outcomes

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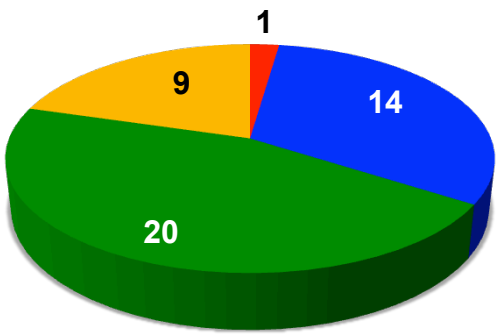
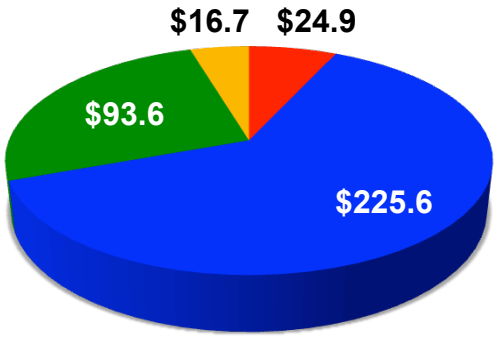
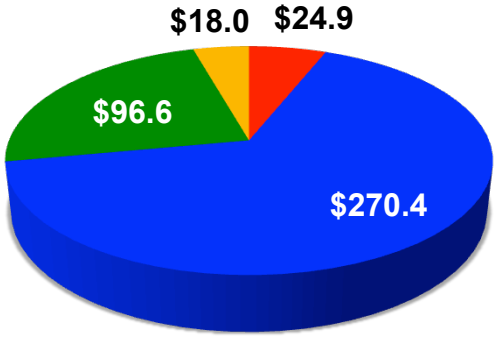
# of Projects
44 awards



CIRM Investment,
$361 MM



CIRM & CFP Investment
$410 MM



Preclinical POC
ET II Awards

DC
ET I, II Awards

IND
DT Awards

Phase I Clinical Study
TCD Award

Translational Portfolio: Stem Cell Source or Target

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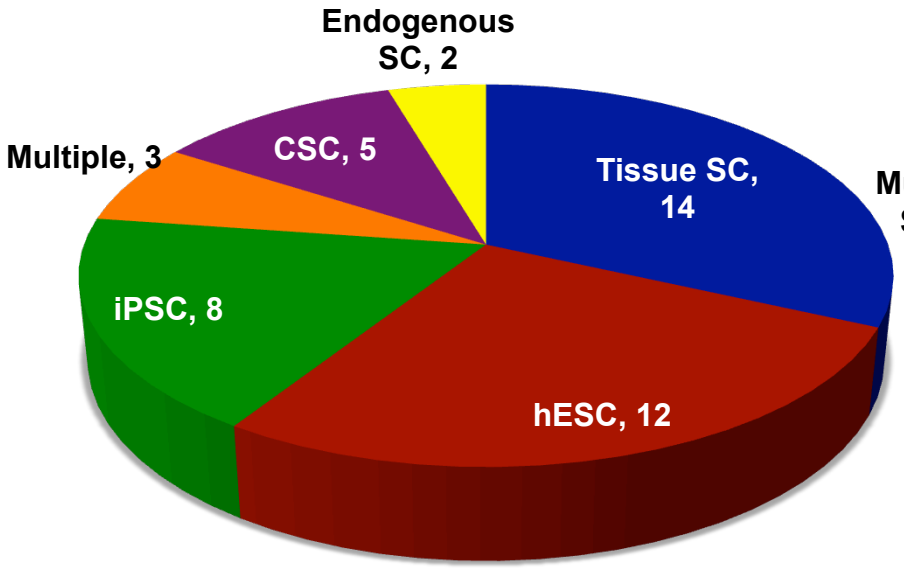
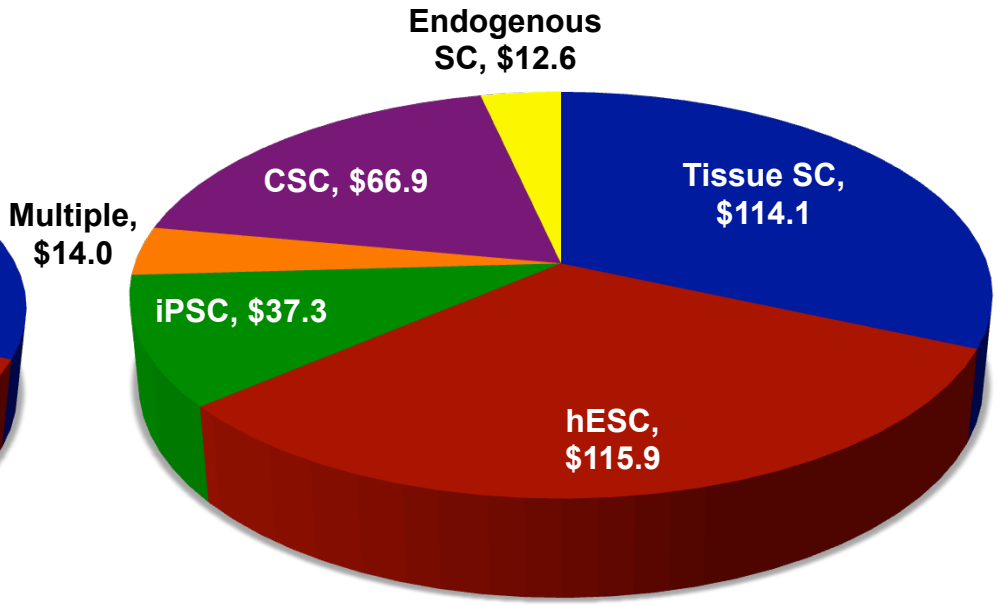
Projects (n = 44)



CIRM Investment ($361 MM)



Stem Cell Source or Target by Program*

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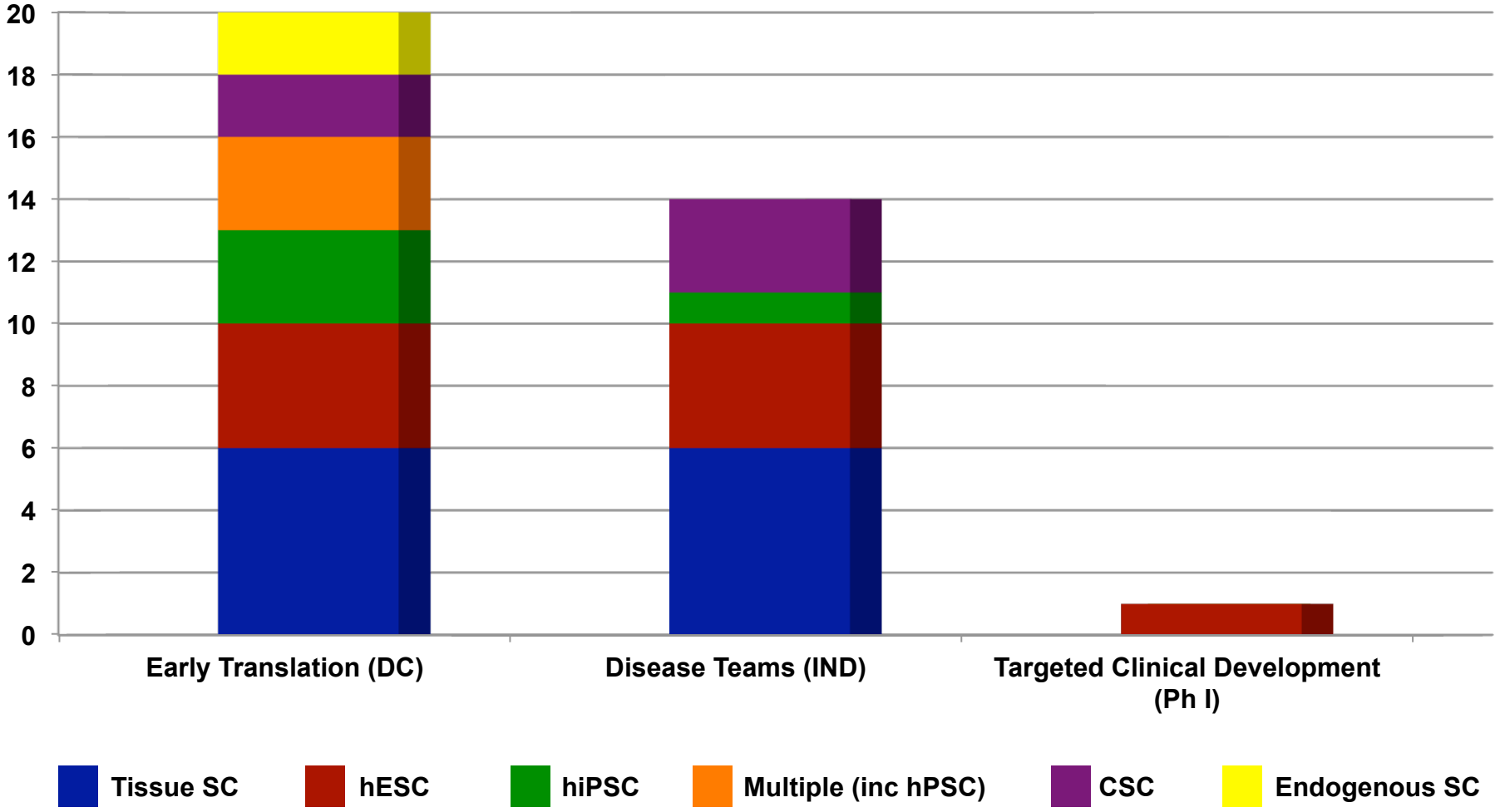

** POC projects not included*

Translational Portfolio: Therapeutic Approach

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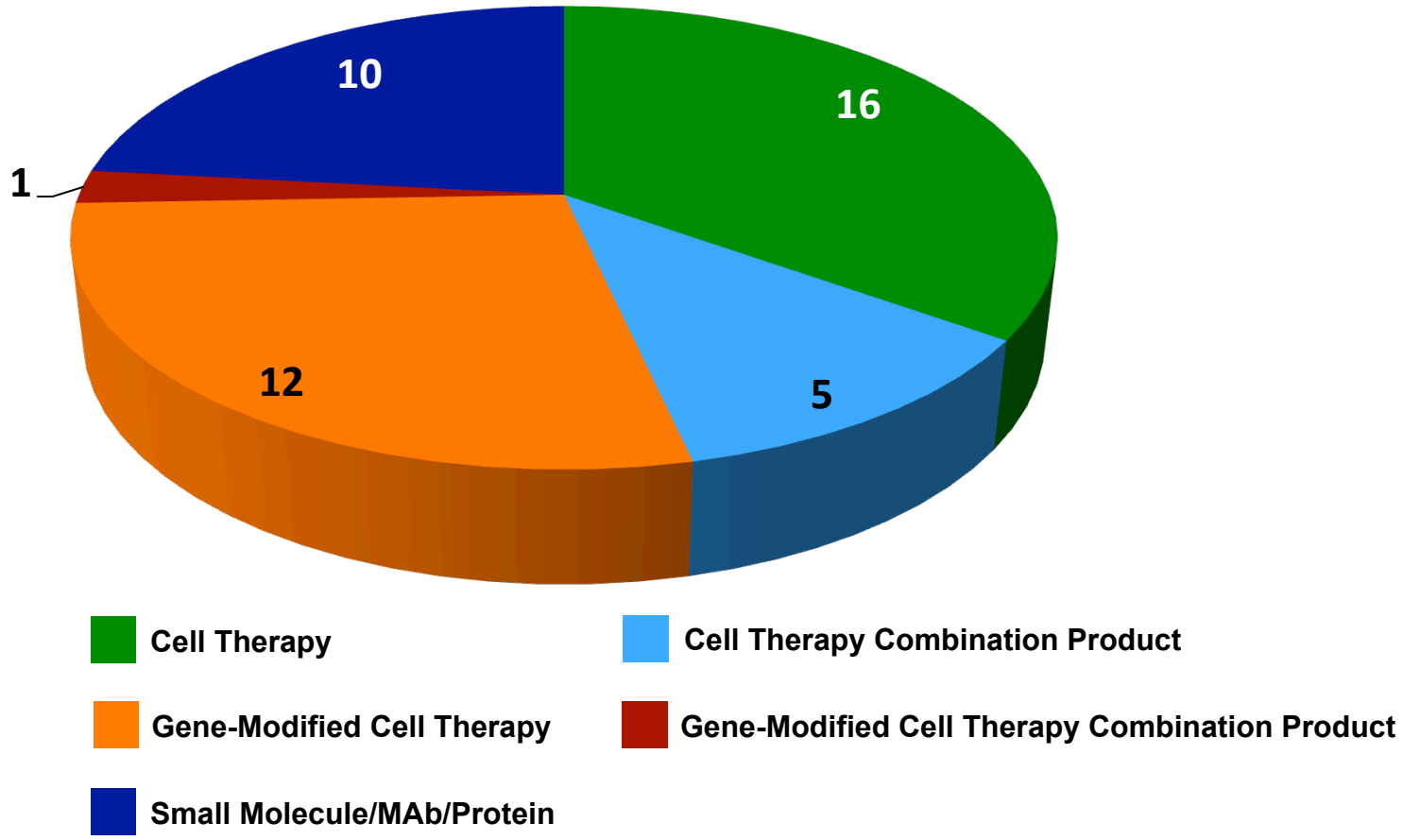
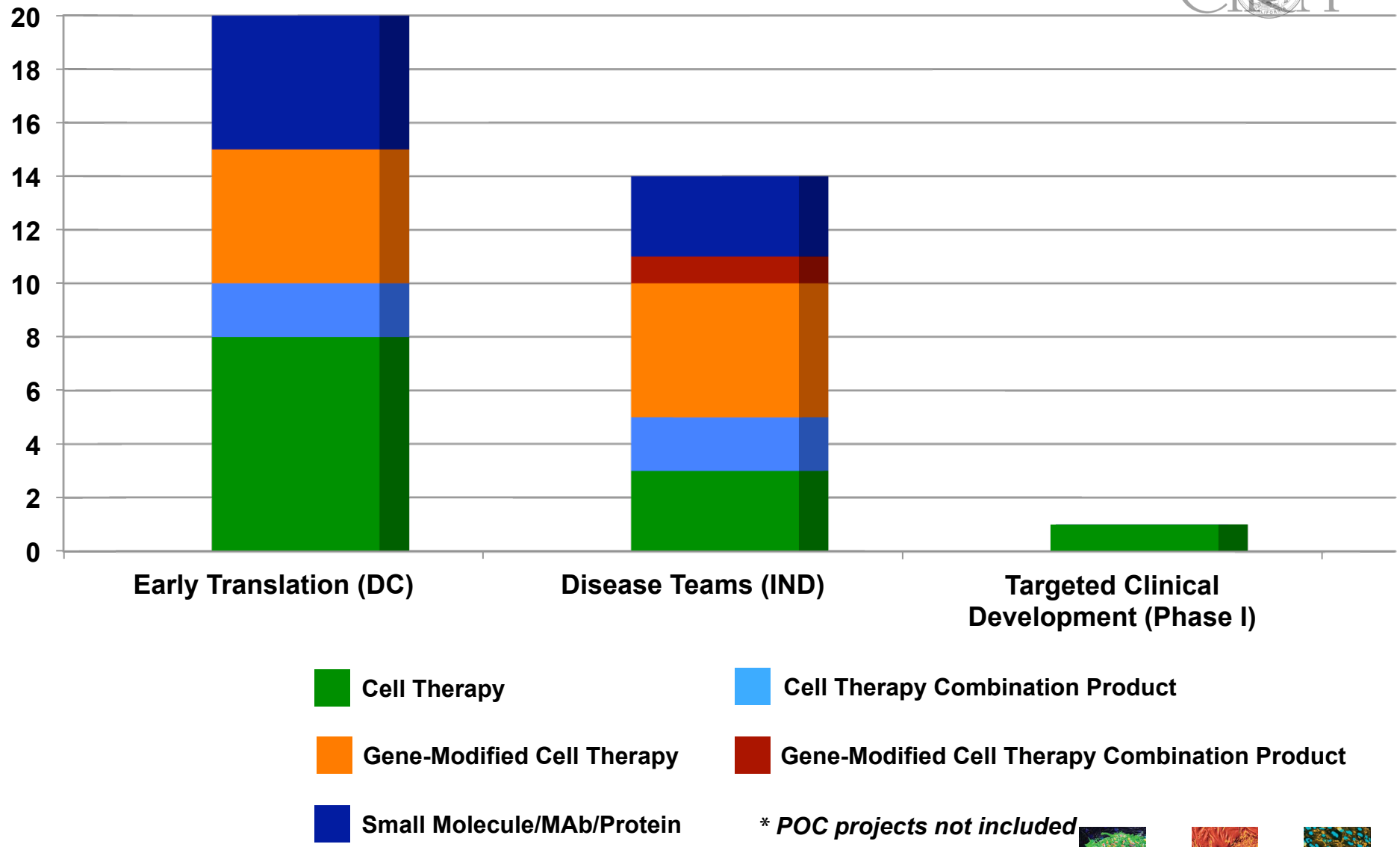
Awards from Early Stage Clinical Trial, Disease Team & Early Translational RFAs



Translational Portfolio: Therapeutic Approach by Program*



Translational Portfolio: Disease

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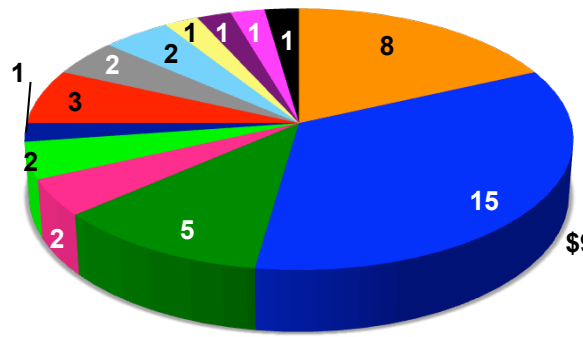
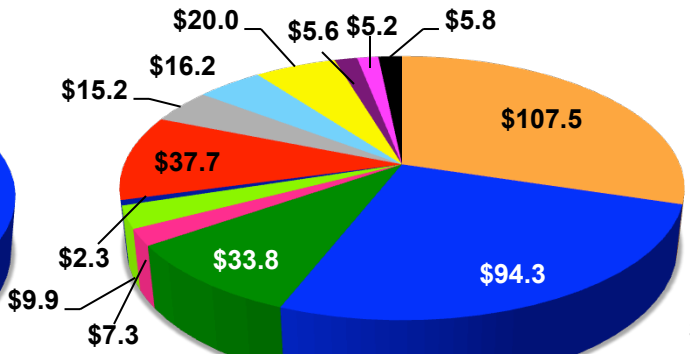
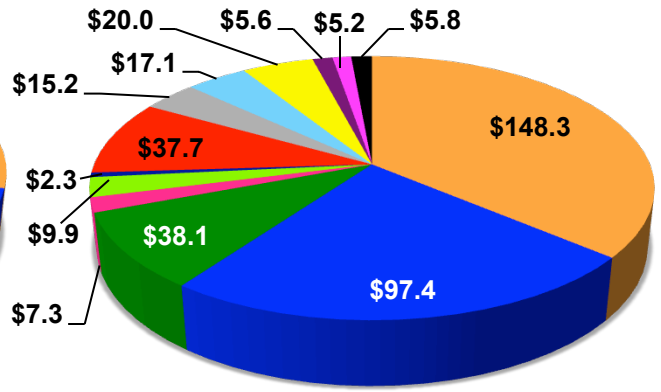
Disease Area, # Projects (n = 44)



Disease Area, CIRM Investment ($361 MM)



Disease Area, CIRM & CFP Investment ($410 MM)



- Cancer
- Neurological Disorders
- Eye Disorders
- Bone Disorders
- Cartilage Disorders
- Skeletal Muscle Disorders
- HIV/AIDS
- Blood Disorders
- Skin Disorders
- Endocrine Disorders
- Heart Disease
- GI/Liver Disorder
- Multiple: Bone Fractures, Wound Healing, Heart Disease, Stroke

Translational Portfolio: Management

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- Disease Teams and Targeted Clinical Development Programs
  - Prior to award
    - mutually agreed upon Go, no go and progress milestones
  - During the conduct of research
    - Interactive ongoing discussions between CIRM Science Officer and Research Team
    - Updates on interval progress on quarterly basis and overall annual progress updates
    - clinical development advisor meetings yearly/ key milestones (DT1 at 12-18 month milestones)
  - CIRM/FDA webinars, educational roundtables, conferences, seminars

Translational Portfolio: Management

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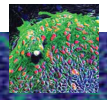
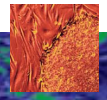
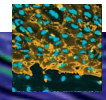
- Early Translational Program
  - Prior to award
    - mutually agreed upon progress milestones and success criteria
  - During the conduct of research
    - Interactive ongoing discussions between CIRM Science Officer and Research Team
    - Updates on interval progress on bi-annual basis and overall annual progress updates
  - CIRM/FDA webinars, educational roundtables, conferences, seminars

Translational Portfolio: Neurological Disorders

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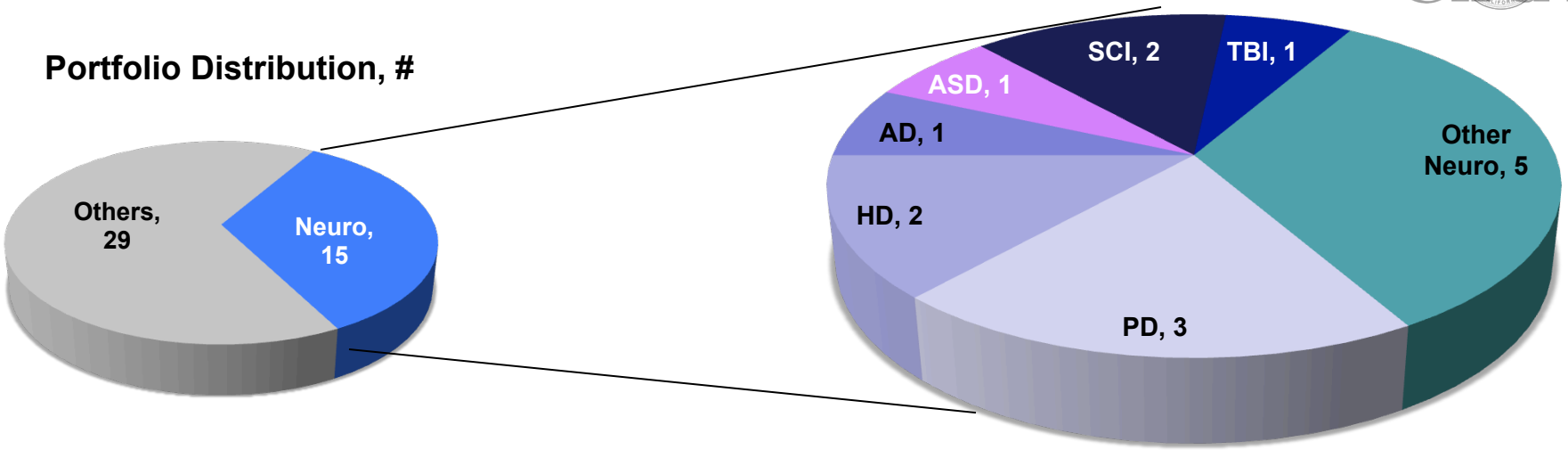
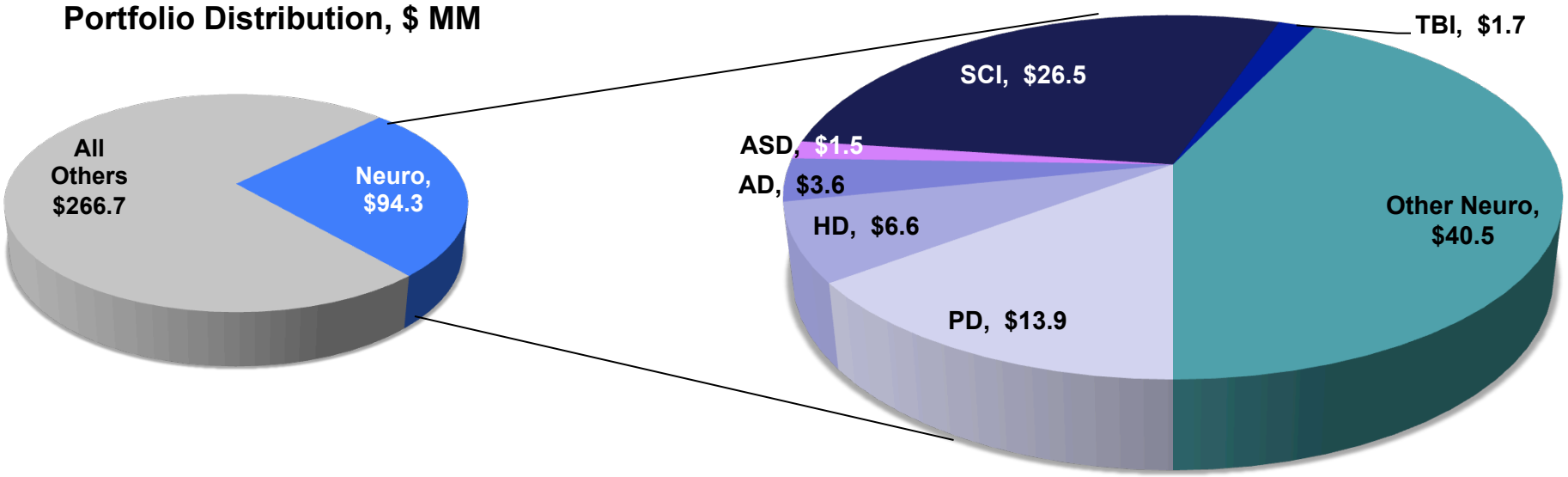
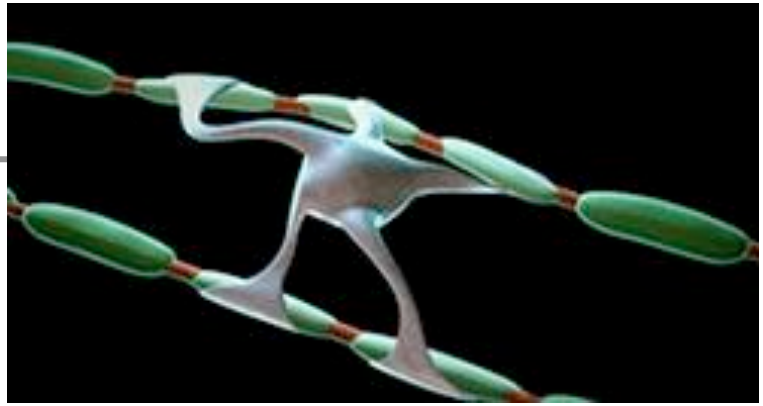




Portfolio: Neurological Disorders - Injury

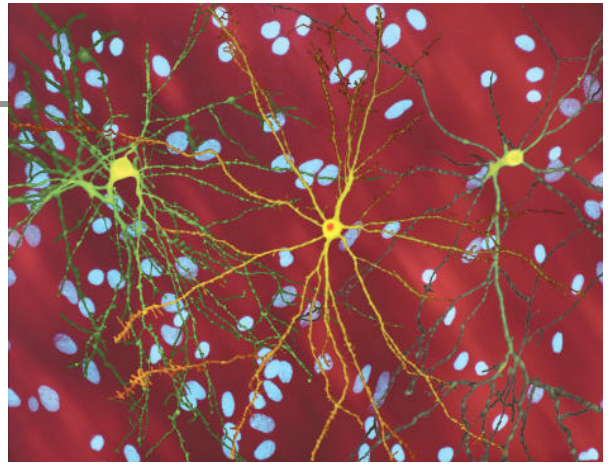


Award	Goal	Injury	Approach
CT1-05168 Geron Corporation	Ph I	Spinal Cord Injury	Allogeneic hESC-derived oligodendrocyte progenitor cells
TR2-01785 UCLA	POC	Spinal Cord Injury	Allogeneic hESC-derived motor and autonomic precursor neurons
DR1-01480 Stanford University, UCLA	IND	Stroke	Allogeneic hESC-derived NSC line transplanted alone or in combination with matrix
TR2-01767 UCI	POC	Traumatic Brain Injury	Allogeneic hESC-derived NSC

Portfolio: Neurological Disorders – Neurodegenerative Disease

Award	Goal	Disease	Approach
DR1-01471 UCSD, Salk Institute	IND	ALS	Allogeneic hESC-derived astrocyte precursors delivered into spinal cord (delivery device)
TR1-01267 Sanford-Burnham Institute; Howard Florey Institute (State of Victoria, AS)	DC	Parkinson's Disease	The best of either hNSC derived from tissue, ESC, or iPSC; or hVM (ventral mesencephalon) precursors derived from ESC, NSC, or tissue
TR2-01856 Buck Institute; City of Hope National Medical Center	DC	Parkinson's Disease	Allogeneic hPSC-derived dopaminergic neurons
TR2-01778 Salk Institute; University of Erlangen (BMBF, Germany)	POC	Parkinson's Disease	Small molecule modulator of neuro-inflammation identified by screening on astrocytes/microglia from patient-derived iPSCs

Portfolio: Neurological Disorders – Neurodegenerative Disease



Award	Goal	Disease	Approach
TR1-01245 UCI, Monash University (State of Victoria, AS)	DC	Alzheimer's Disease	Allogeneic hESC-derived NSC or hESC-derived NSC genetically modified with a beta-amyloid degrading enzyme or a transcription factor that promotes neuronal differentiation for transplantation
TR1-01257 UCD	DC	Huntington's Disease	Allogeneic MSC engineered ex vivo to express siRNA targeting mutant huntingtin mRNA. Injected intracranially
TR2-01841 UCI	DC	Huntington's Disease	Allogeneic hESC-derived neural stem or progenitor cells for transplantation

Portfolio: Neurological Disorders

Award	Goal	Disease	Approach
TR2-01844 iPierian, Inc.	DC	Spinal Motor Atrophy	Small molecule that increases SMN1 gene product in patient iPSC-derived motor neurons
TR2-01832 City of Hope National Medical Center, University of Bonn (BMBF, Germany)	POC	Canavan Disease	Autologous iPSC-derived neural or oligodendrocyte progenitors, genetically modified to correct mutant (aspartoacylase) ASPA gene
TR2-01814 UCSD	POC	Autism Spectrum Disorders	Neurons from ASD (and control) iPSC for phenotype screening, assay development and validation, drug screening and biomarker identification
TR2-01749 UCSD	POC	Refractory Epilepsy	Allogeneic hESC-derived progenitors from GABAergic inhibitory neurons analogous to those in medial ganglionic eminence

Translational Portfolio: Eye Disorders

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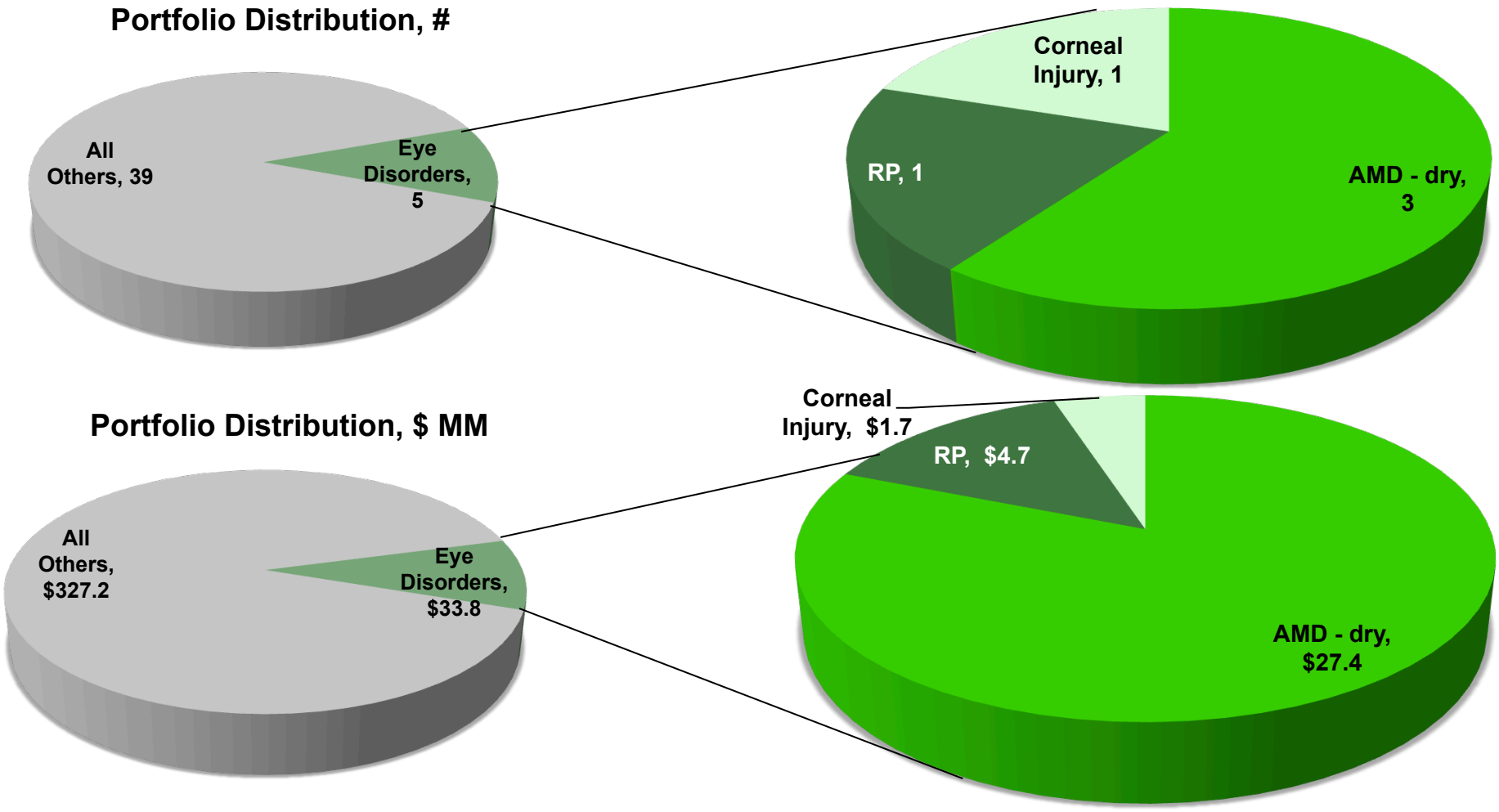

Portfolio: Eye Disorders

Award	Goal	Disease	Approach
DR1-01444 USC, UCSB, University College London (MRC, UK)	IND	Age-related Macular Degeneration (Dry form)	Allogeneic functionally polarized hESC-derived RPE monolayers on synthetic substrate implanted sub-retinally
TR1-01219 Scripps Research Institute	DC	Age-related Macular Degeneration (Dry form)	Autologous iPSC-derived RPE (generated without integrating vectors)
TR1-01272 UCLA	DC	Age-related Macular Degeneration (Dry form)	Autologous adult SC (CMZ) or iPSC-derived RPE +/- *ex vivo* engineering to express negative regulators of complement cascade
TR2-01794 UCI	DC	Retinitis Pigmentosa	Allogeneic retinal progenitor cells
TR2-01768 UCLA	POC	Corneal Injury	*Ex vivo* expansion of corneal epithelial stem/progenitor cells, also known as limbal stem cells

Translational Portfolio: Cancer

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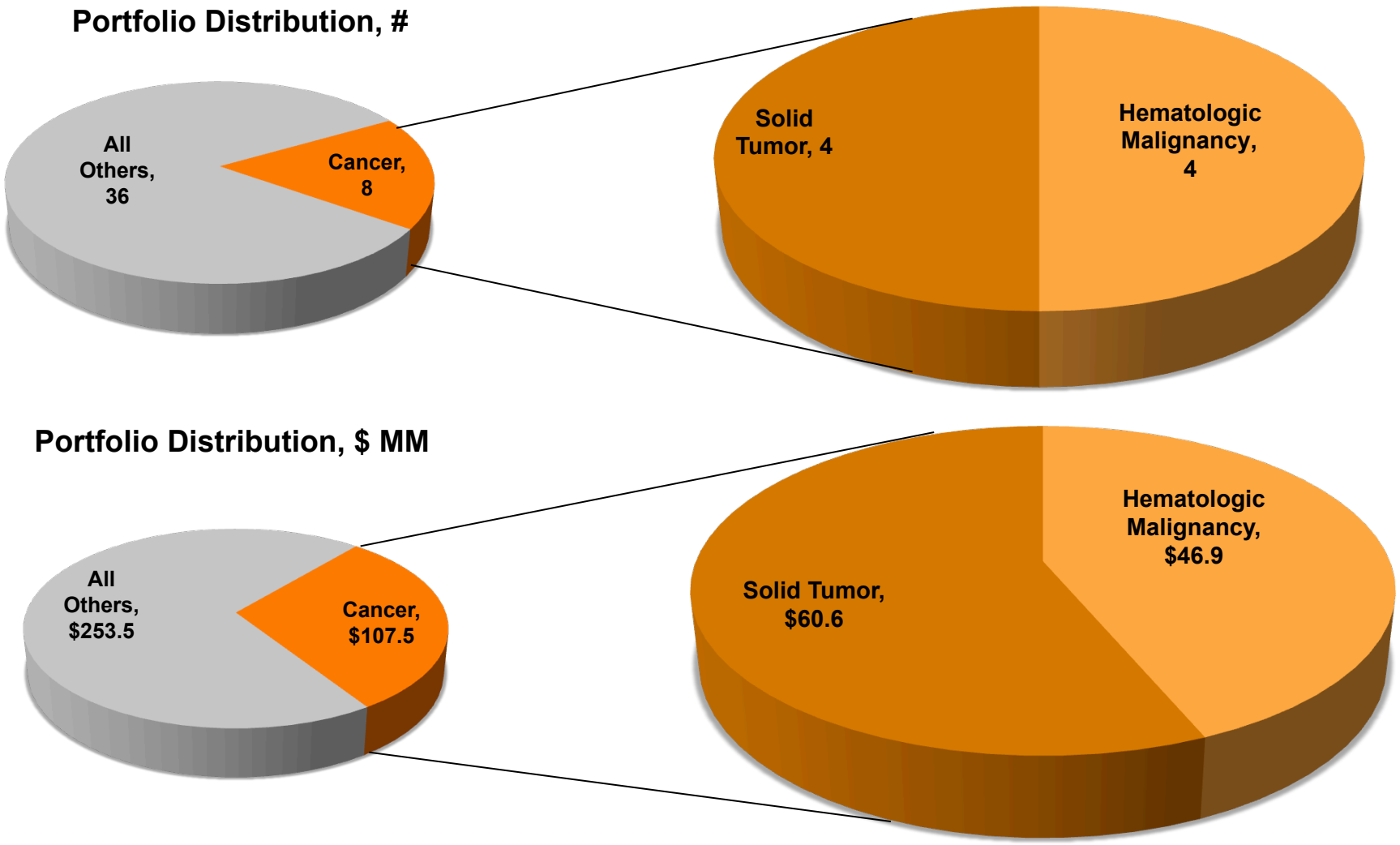
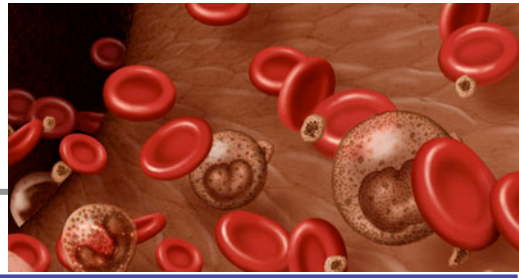
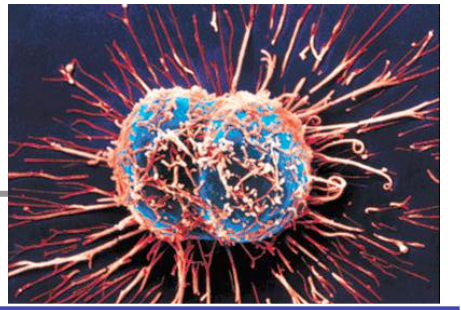


Portfolio: Cancer – Hematologic Malignancy



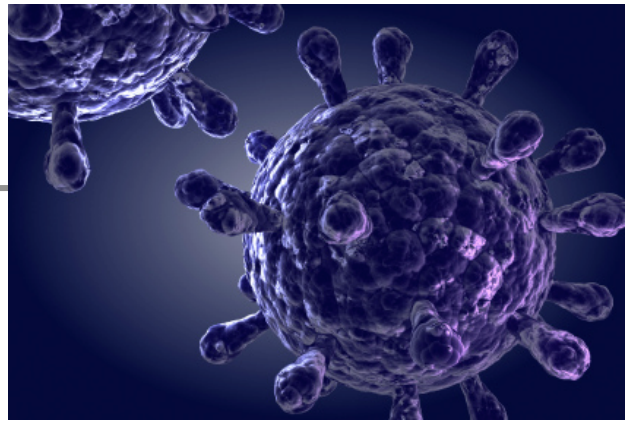
Award	Goal	Disease	Approach
DR1-01430 UCSD, University Health Network (CSCC, Canada)	IND	AML, CML, ALL, CLL	Existing candidate molecules (3 small molecule, 3 MAb) targeting leukemic stem cells (LSC) by blocking survival and self-renewal pathways that function preferentially in human LSC compared to normal HSC
DR1-01485 Stanford University; Weatherall Institute, Oxford University (MRC, UK)	IND	AML	Monoclonal antibody against CD47 – "Don't eat me" antigen that is expressed on LSC and inhibits their phagocytosis by macrophages
TR2-01789 UCSD	DC	CML	Small molecule pan BCL-2 inhibitor targeting cancer stem cells
TR2-01816 Children's Hospital of L.A., University of Jena (BMBF, Germany)	DC	AML, ALL	Small molecule inhibitor of BCL6 targeting cancer stem cells

Portfolio: Cancer – Solid Tumor



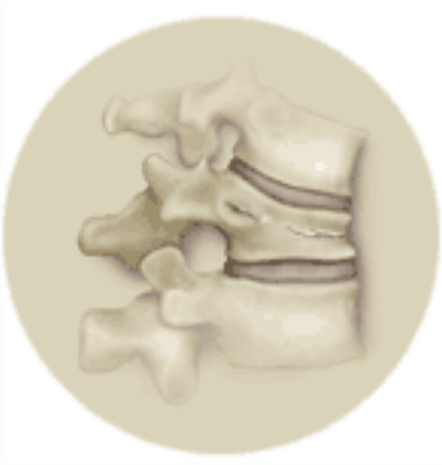
Award	Goal	Disease	Approach
DR1-1477 UCLA; Stanford University, USC, University Health Network (CSCC, Canada)	IND	Colon cancer, ovarian cancer, glioblastoma	Small molecules specific for each of two drug targets in cancer stem cells
DR1-01421 City of Hope National Medical Center	IND	Glioblastoma	Allogeneic hNSC line to target tumor, engineered ex vivo to deliver carboxylesterase to locally convert CPT-11 to more potent SN-38
DR1-01426 UCSF, Ludwig Institute for Cancer Research, Sanford-Burnham Institute	IND	Glioblastoma	Allogeneic hNSC, either of two lines, or hMSC to target tumor, engineered ex vivo to deliver a tumorcidal gene product, TRAIL or cytosine deaminase, and a suicide gene
TR2-01791 UCLA	DC	Glioblastoma	Tumor homing by allogeneic hMSC genetically engineered to produce replication competent retrovirus encoding a suicide gene

Portfolio: HIV/AIDS



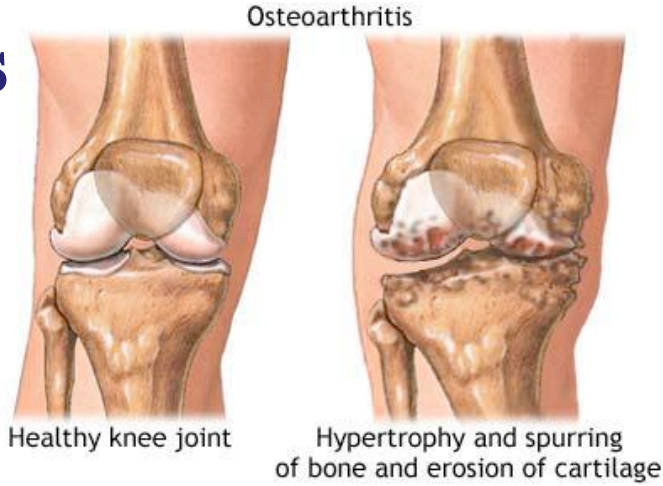
Award	Goal	Disease	Approach
DR1-1431 UCLA, Calimmune, Inc.	IND	AIDS Lymphoma	Autologous HSC transduced *ex vivo* with a lentiviral vector engineered to express a shRNA against CCR5 & fusion inhibitor. IV administration after myeloablation.
DR1-1490 City of Hope National Medical Center, USC, Sangamo Biosciences	IND	AIDS Lymphoma	Autologous HSC transduced *ex vivo* with non-integrating vector engineered to express zinc finger nuclease against CCR5. IV administration after myeloablation
TR2-1771 City of Hope National Medical Center	DC	AIDS Lymphoma	Autologous HSC genetically modified *ex vivo* with multiple anti-HIV resistance genes and a drug resistance gene

Portfolio: Bone Disorders



Award	Goal	Disease	Approach
TR2-01821 UCLA	DC	Bone Disorder: Spinal fusion	Autologous adult perivascular stem cells and an osteoinductive protein on a FDA-approved acellular scaffold
TR2-01780 Cedars-Sinai Medical Center	POC	Bone Disorder: Osteoporosis-related vertebral compression fractures	MSCs in combination with parathyroid hormone (PTH)

Portfolio: Cartilage Disorders

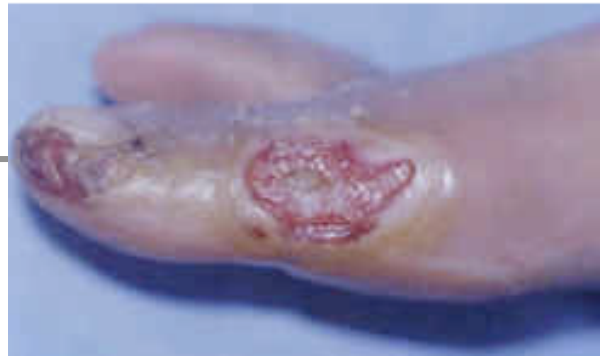


Award	Goal	Disease	Approach
TR1-01216 Scripps Research Institute	DC	Focal cartilage defect, Osteoarthritis	iPSC- or ESC derived chrondrocyte progenitors implanted into chrondral defect or injected into OA joint
TR2-01829 Scripps Research Institute	DC	Osteoarthritis	Optimized small molecule of lead molecule PRO1 that induces chondrocyte differentiation of resident MSC

Portfolio: Blood & Genetic Disorders

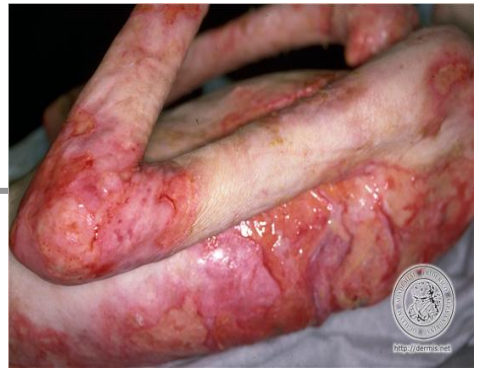
Award	Goal	Disease	Approach
DR1-01452 UCLA, Children's Hospital, LA	IND	Sickle Cell Anemia	Autologous HSC, genetically corrected *ex vivo* by lentiviral vector mediated addition of a hemoglobin gene that blocks sickling. IV administration after myeloablation
TR1-01273 Salk Institute	DC	Fanconi Anemia, X-SCID	Autologous iPSC-derived HSC genetically corrected by homologous recombination

Portfolio: Diabetes & Complications



Award	Goal	Disease	Approach
DR1-01423 ViaCyte Inc., UCSF	IND	Diabetes	Allogeneic hESC-derived pancreatic cell progenitors in a device implanted subcutaneously that mature *in vivo* to beta cells that secrete insulin in response to glucose. Transient immunosuppression.
TR2-01787 UCD, Technical University of Munich (BMBF, Germany)	DC	Chronic diabetic foot ulcers	Allogeneic hMSCs on a dermal regeneration scaffold

Portfolio: Other Candidate Therapeutics



Award	Goal	Disease	Approach
DR1-01454 Stanford University	IND	Dystrophic Epidermolysis Bullosa	Epidermal sheets from expanded autologous genetically corrected (to express wild type COL7A1) iPSC-derived keratinocytes
DR1-01461 Cedars-Sinai Med. Center	IND	Advanced Ischemic Cardiomyopathy (heart failure)	Autologous cardiac derived, 'cardiospheres', expanded and delivered by direct catheter injection into heart muscle
TR1-01249 Stanford University	DC	Multiple (Stroke, Heart disease, Skin ulcers, Bone fractures)	Recombinant Wnt in a sustained release formulation to stimulate endogenous stem cells to repair tissues
TR2-01857 UCD, UCSF	DC	Liver failure	Allogeneic genetically modified hESC-derived hepatocytes
TR2-01756 Stanford University	POC	Duchenne muscular dystrophy	Autologous skeletal muscle precursor cells derived from human iPSCs genetically modified to correct the dystrophin gene

Take Home Points

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

- Substantive progress in strengthening and expanding the translational portfolio over the past 18 months
  - Investments in numbers and dollars in programs moving towards and into clinical trials across a spectrum of therapeutic areas in chronic, debilitating diseases and injuries
  - Investments across stem cell platforms
- Working collaboratively with funding partners across US and internationally to leverage expertise and resources
- Forging interactions with FDA and companies to clarify pathway for progress towards patients
- Active management of research programs with predefined criteria for milestones, ongoing interactive dialog and facilitated interactions