AAWG
Clinical Portfolio Update

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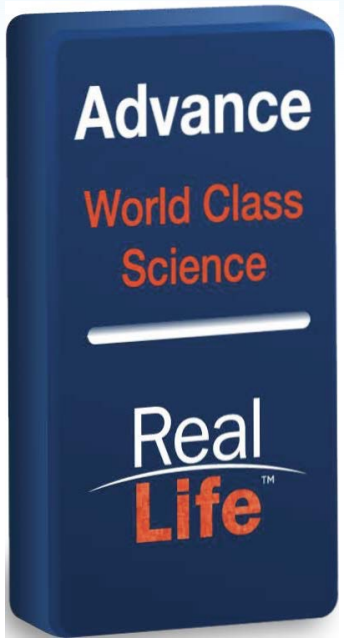
CIRM
CALIFORNIA'S STEM CELL AGENCY

Our Mission

OUR MISSION

Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

5-Year Strategic Summary



- Develop Competency Hubs
- Build Knowledge Networks

- **Advance therapies to marketing approval**
- Create a manufacturing partnership network
- Expand Alpha Clinics Network
- Create Community Care Centers of Excellence

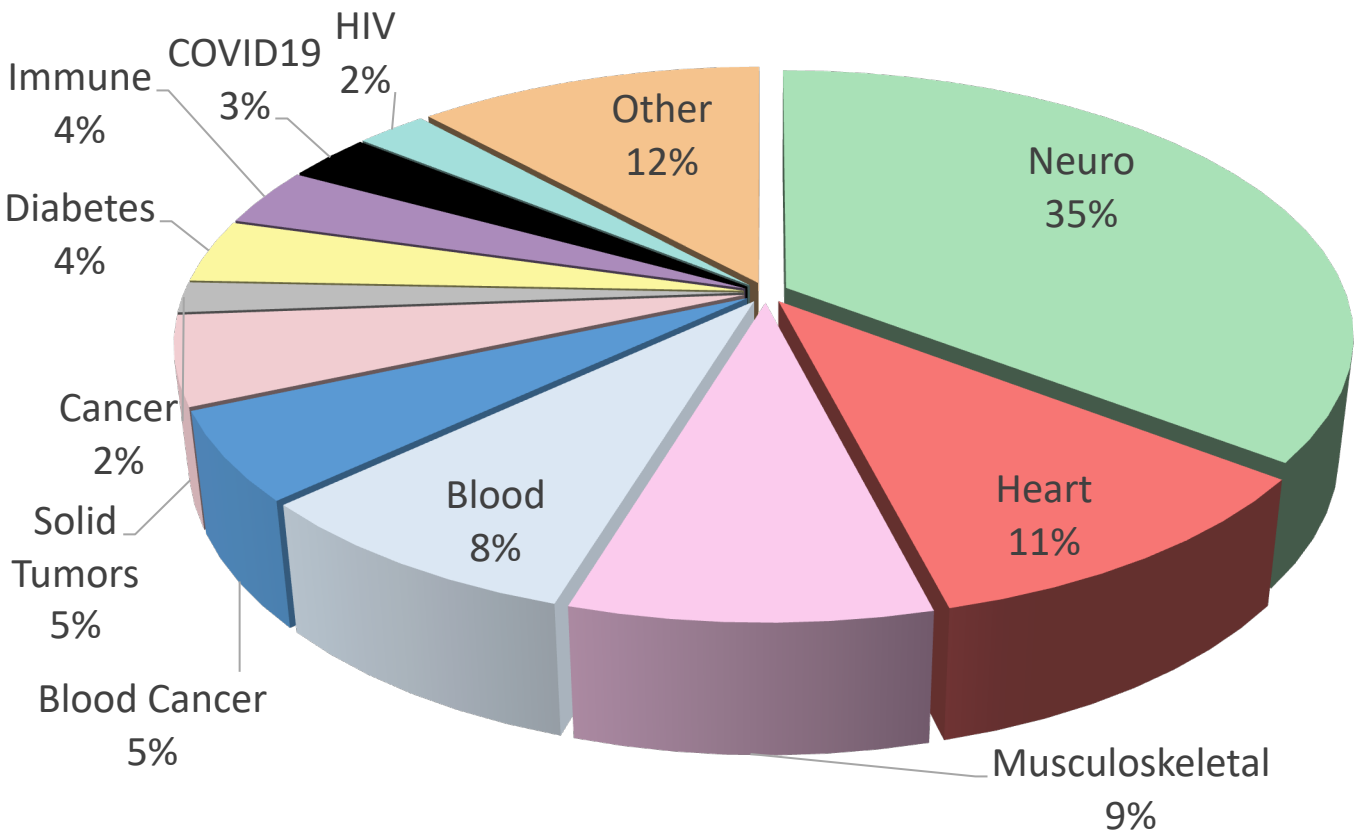
- Build a diverse and highly skilled workforce
- Deliver a roadmap for access and affordability

Translational and Clinical Portfolio Phases

Pre-IND Meeting Prep	IND-Enabling	Early Clinical	Mid-Clinical	Pivotal-Late Clinical
35.5%	11.2%	34.6%	13.1%	5.6%

81.3% of our current portfolio = de-risking projects

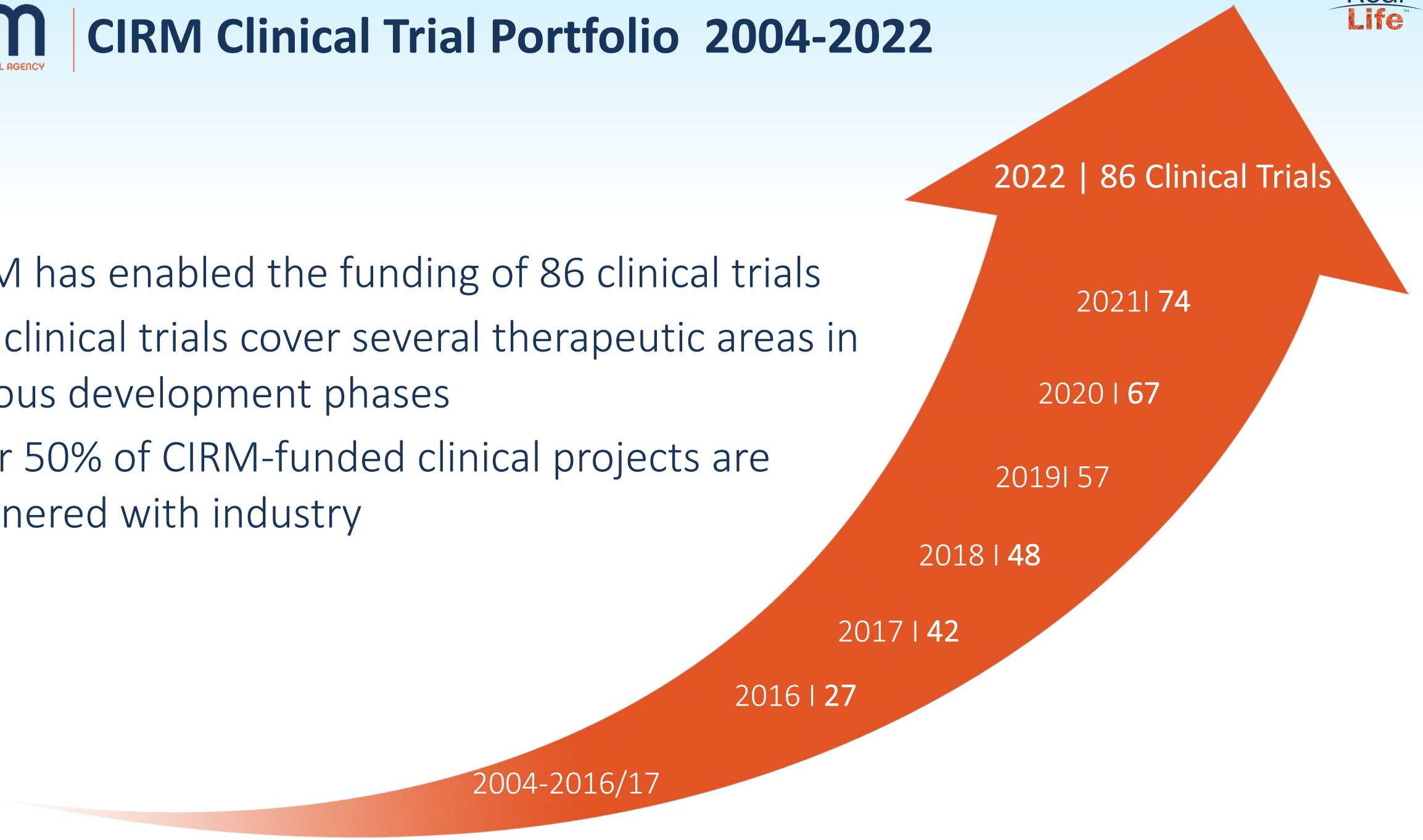
As of September 2022.
% Total R&D awards



Updated: Dec 2022

CIRM Clinical Trial Portfolio 2004-2022

- CIRM has enabled the funding of 86 clinical trials
- The clinical trials cover several therapeutic areas in various development phases
- Over 50% of CIRM-funded clinical projects are partnered with industry



CIRM Active Trials | Phase 1

Disease Areas	Investigator	Organization	Trial Status	Target Enrollment
Blood disorder	Tippi MacKenzie	University of California, San Francisco	Enrolling by invitation	10
Neurobiology	Clive Svendsen	Cedars-Sinai Medical Center	Recruiting	16
Blood cancer	David Miklos	Stanford University	Recruiting	60
Blood cancer	Maria Grazia Roncarolo	Stanford University	Recruiting	22
Urinary disorder	James Yoo	Wake Forest University Health Sciences	Launching	10
Solid cancer	Christine Brown	City of Hope, Beckman Research Institute	Active, not recruiting	82
Solid cancer	Jana Portnow	City of Hope, Beckman Research Institute	Launching	36
Solid cancer	Saul Priceman	City of Hope, Beckman Research Institute	Recruiting	39
Solid cancer	Leo Wang	City of Hope, Beckman Research Institute	Recruiting	18
Solid cancer	Crystal Mackall	Stanford University	Recruiting	54
Ophthalmology	Sophie Deng	University of California, Los Angeles	Recruiting	20
Infectious disease	John Zaia	City of Hope, Beckman Research Institute	Active, not recruiting	N/A
Neurobiology	Cory Nicholas	Neurona Therapeutics	Recruiting	40
Cardiovascular	Joseph Wu	Stanford University	Recruiting	18
Infectious disease	William Kennedy	Excision BioTherapeutics	Recruiting	9

CIRM Active Trials | Phase 1 (Cont'd)

Disease Areas	Investigator	Organization	Trial Status	Target Enrollment
IPEX Syndrome	Rosa Bacchetta	Stanford University	Recruiting	36
Transplant	Robert Lowsky	Stanford University	Recruiting	15
Transplant	Everett Meyer	Stanford University	Recruiting	22
Blood cancer	Joseph Woodard	Immune-Onc Therapeutics	Recruiting	119
Solid cancer	Steven Dubinett	University of California, Los Angeles	Recruiting	24
Neurobiology	Krystof Bankiewicz	Brain Neurotherapy Bio	Recruiting	12
Blood disorder	Donald Kohn	University of California, Los Angeles	Recruiting	6
Ophthalmology	Clive Svendsen	Cedars-Sinai Medical Center	Recruiting	16
Solid cancer	Theodore Nowicki	University of California, Los Angeles	Recruiting	12
Blood disorder	Morton Cowan	University of California, San Francisco	Recruiting	25
Blood disorder	Joseph Rosenthal	City of Hope, Beckman Research Institute	Recruiting	6
Blood disorder	Mark Walters	University of California, San Francisco	Launching	9
Solid cancer	Pamela Contag	BioEclipse Therapeutics INC.	Recruiting	24
Neurobiology	Diana Farmer	University of California, Davis	Recruiting	55
Neurobiology	Gary Steinberg	Stanford University	Recruiting	30

CIRM Active Trials | Phase 1/2

Disease Areas	Investigator	Organization	Trial Status	Target Enrollment
Infectious disease	Michael Pulsipher	Children's Hospital of Los Angeles	Active, not recruiting	60
Infectious disease	William van der Touw	Cellularity Inc	Active, not recruiting	86
Cystinosis	Stephanie Cherqui	University of California, San Diego	Recruiting	6
Blood cancer	Mehrdad Abedi	University of California, Davis	Recruiting	18
Infectious disease	Steven Deeks	University of California, San Francisco	Recruiting	12
Blood disorder	Kinnari Patel	Rocket Pharmaceuticals, Inc.	Active, not recruiting	9
Blood disorder	Stephen Gottschalk	St. Jude Children's Research Hospital	Recruiting	28
Blood disorder	Donald Kohn	University of California, Los Angeles	Recruiting	16
Muscle	Peter Belafsky	University of California, Davis	Recruiting	62
Cardiovascular	Michael Lewis	Cedars-Sinai Medical Center	Active, not recruiting	26
Type 1 diabetes	Peter Stock	University of California, San Francisco	Recruiting	8
Type 1 diabetes	Manasi Jaiman	ViaCyte, Inc.	Active, not recruiting	75

CIRM Active Trials | Phase 2

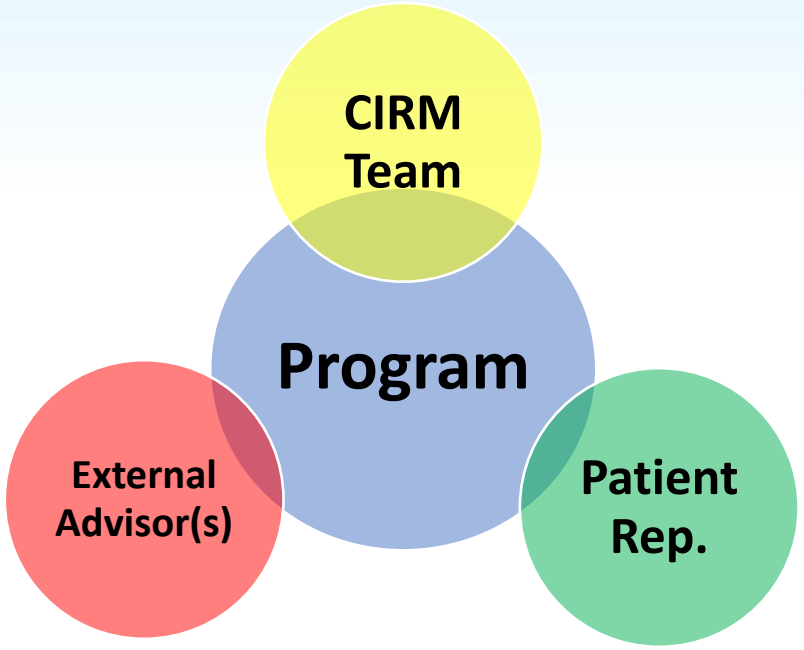
Disease Areas	Investigator	Organization	Trial Status	Target Enrollment
Infectious disease	Michael Matthay	University of California, San Francisco	Recruiting	120
Ophthalmology	Henry Klassen	jCyte, Inc	Active, not recruiting	84
Ophthalmology	Henry Klassen	jCyte, Inc	Active, not recruiting	35
Blood disorder	David Williams	Boston Children's Hospital	Recruiting	10

CIRM Active Trials | Phase 3

Disease Areas	Investigator	Organization	Trial Status	Target Enrollment
Neurobiology	Ralph Kern	BrainStorm Cell Therapeutics	Active, not recruiting	263
Transplant	Daniel Brennan	Medeor Therapeutics, Inc.	Active, not recruiting	30
On Vascular Niche	Finnegan	Angiocrine	Active, recruiting	140

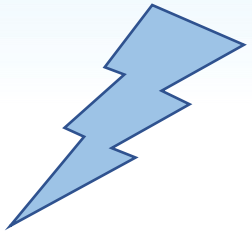
Clinical Advisory Panels (CAPs)

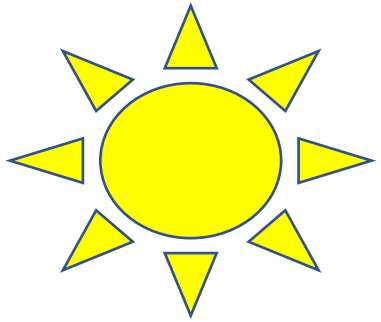
- **Purpose** of a **CAP** is to provide guidance and advice to the project team
- A **CAP** is assembled by CIRM for each Clinical Stage Award
- Multiple **CAP Meetings** occur over lifetime of a program award



- 356 CAP meetings since 2016
- 91 External advisors
- 68 Patient representatives

CAPs Make a Difference





- Resolving challenges
- Optimizing project execution
- Discovering critical information
- Strategic, Technical, Regulatory Guidance

Outcomes:

- Manufacturing challenges overcome
- Clinical trial design optimized
- Enrollment enhanced
- Regulatory advice provided
- Partnering facilitated
- Development Path delineated

CAP advice impacted >75% of CLIN awards

Cell Therapy for Retinitis Pigmentosa

Orphan & Accelerated FDA Designation (RMAT)*

PI: Henry Klassen, UC Irvine and jCyte

Phase 2 trial using human retinal progenitor cells (jCell) injected intravitreally

Rationale

- The program is focused on the development of human retinal progenitor cells for treatment of the blinding retinitis pigmentosa (RP).

Status

- The phase 2 study identified a “biomarker” a central visual field diameter greater than 20 degrees responded well to jcell
- The current **retreatment** clinical trial enrollment is complete 35 patients
- Design of potential registration trial is in progress

Rosie

*RMAT: Regenerative Medicine Advanced Therapy

Autologous Ex Vivo Lentiviral Gene Therapy for Adenosine Deaminase (ADA) Deficiency

PI: Donald Kohn
UCLA

Orphan, Accelerated FDA Designation
Breakthrough & Rare Pediatric Disease

Evie

Rationale

- Gene therapy composed of the patient's hematopoietic stem and progenitor cells (HSPCs) transduced ex vivo with viral vector encoding human *ADA* gene.

Status

- Enrolled fifty patients with ADA-SCID (30 in the United States and 20 in the United Kingdom)
- Data from the two U.S. studies at 24 months of follow-up were analyzed alongside data from the U.K. study at 36 months of follow-up are promising.
- A clinical trial to be conducted by Dr. Kohn has been given the go-ahead by the FDA
- Recruitment starting in early 2023, with enrollment beginning shortly thereafter.

EX vivo Lenti-viral Gene therapy- LADI CELL

Orphan & Accelerated FDA Designation (RMAT)

PI: K. Patel
Rocket Pharma

Rationale

- Patient's hematopoietic cells are transduced ex vivo with a viral vector carrying a functional copy of the CD18 gene.

Status

- Promising results with 9 patients **
  - "Reported 100% overall survival at 12-months post infusion
  - Significant reduction in all hospitalizations, infection- and inflammatory-related hospitalizations
  - "Data also shows evidence of resolution of skin rash and restoration of wound repair capabilities."

- "Based on the phase 2 results, Rocket Pharma initiated discussions with health authorities on filing plans"

Marley

*RMAT: Regenerative Medicine Advanced Therapy
** (Rocket pharma Press release May 19, 2022)

Cell Therapy for Kidney Transplants- Orphan & Accelerated FDA Designation (RMAT)*

PI: Dr. Brennan Medeor

Cellular Immunotherapy for Induction of Immune Tolerance in HLA Matched Living Donor Kidney Transplant Recipients

Rationale

- The goal is to induce tolerance to transplanted kidneys via transplant of specific hematopoietic stem cells from the kidney donor.

Status

- Study enrolled a total of 30 patients (20 treated , 10 control)
- Patient two year follow up is ongoing

*Press Release: 09.22.2020 Medeor Therapeutics' Transplant Immune Tolerance Therapy Receives Regenerative Medicine Advanced Therapy (RMAT) Designation from FDA

A monoclonal antibody that depletes blood stem cells and enables chemotherapy free transplants in severe combined immunodeficiency(SCID)

Orphan, Rare Pediatric Disease, & Fast Track FDA Designation*

PI: Ping Wang
Jasper Therapeutics

Rationale

- Patients with the bubble boy disease (SCID) cannot fight infections because their stem cells do not make immune cells/ T cells and B cells
- The humanized monoclonal antibody results in a niche space in the bone marrow which gets repopulated by the transplant of normal donor stem cells resulting in normal levels of T and B lymphocytes that cure them of their disease

Status

Promising results: **

- Single-Agent Conditioning with the antibody shows donor engraftment, naïve lymphocyte production, and clinical benefit in SCID patients

* Jasper Press Release September 15, 2022
** Jasper Press Release March 31, 2022

Endothelial Cell AB-205 therapy in Lymphoma patients Undergoing High-Dose Therapy and Autologous Hematopoietic Cell Transplantation

PI: Paul Finnegan
Angiocrine

RMAT Accelerated FDA Designation*

Rationale

- Administration of endothelial cells as a therapeutic to lymphoma patients undergoing High-Dose chemotherapy and Autologous Hematopoietic Cell Transplantation to reduce the damage to healthy bystander tissues and minimize severe regimen-related toxicities

Status

- Completed Phase 1b/2 study demonstrated preliminary safety and efficacy of the endothelial cells in Lymphoma patients undergoing high dose chemotherapy and autologous hematopoietic cell transplantation.
- The Phase 1b/2 study also provided the justification for a single Phase 3 dose.
- This phase 3 trial was recently funded by CIRM**

*RMAT: Regenerative Medicine Advanced Therapy Angiocrine biosciences Press Release Nov 21, 2020
** Angiocrine Biosciences Press release Dec 22, 2022

In Utero Cell Therapy for Spina Bifida

PI: Diana Farmer, UC Davis

Phase 1/2 trial in newborns *in utero* using a stem cell matrix

Rationale

- Spina Bifida - damage to the spinal cord and nerves and paralysis due to failure of neural tube closure.
- Moderate results with primary closure (MOMS trial)

Status: CuRe Trial

- Placental stem cells on amniotic membrane patch for dura replacement . Pilot study with 6
- 3 infants treated thus far
- 10 month evaluations pending; 6 year follow-up

Baby Toby at his 3-month exam
With Mom Michelle & Dad Jeff

Phase 2 Study of Hematopoietic Stem Cell Gene Transfer Inducing Fetal Hemoglobin in Sickle Cell Disease

PI: D. Williams
Dana Farber

Rationale

- Using the patient's own stem cells genetically engineered to reduce sickle hemoglobin stably and permanently while simultaneously inducing the fetal hemoglobin in red blood cells of affected individuals.

Status

- Clinical site activation and patient recruitment started in California & other US sites
- Tech Transfer manufacturing to California has been successful

Conclusions

- Translation & Clinical Portfolio is diverse, covers multiple Therapeutic areas
- Several of the clinical grants are in early development consistent with CIRM de-risking development
- The Translational and Clinical Advisory Panels resolved several technical, regulatory and strategic challenges and facilitated partnerships.
- Eight grants progressed to later stage development working closely with CIRM with half of them repeat grants over several years for the same project.

Thank You!

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www.cirm.ca.gov