September 2017

CIRM 2.0

CALIFORNIA'S STEM CELL AGENCY

Clinical Program Review

September 2017

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Associate Director, Therapeutics

Accelerating and Developing a Robust Clinical Program

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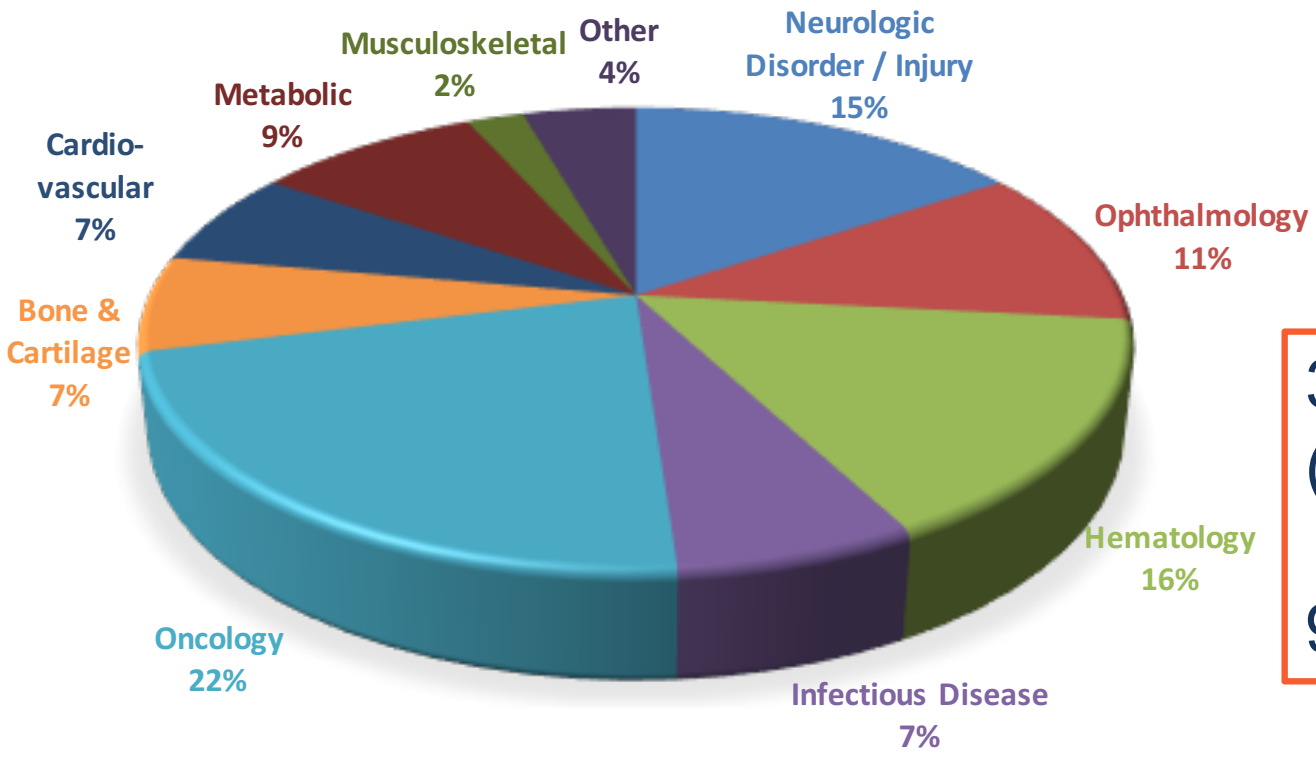
Diverse Therapeutics Portfolio



35 Clinical Trials
(30 active)

9 Preparing IND

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CIRM-Funded Clinical Trials

Stem Cell Gene Therapy

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Clinical Trials

Stem Cell Gene Therapy Program Status

Indication	Investigator / Organization	Phase	Status	Targeted Enrollment
Advanced Malignancies	**Ribas/UCLA**	**Phase 1**	**Initiating**	**12**
Chemotherapy-free transplantation (X-linked SCID)	**Shizuru/Stanford**	**Phase 1/2a**	**Enrolling**	**40**
ADA-SCID	**Kohn / UCLA**	**Phase 2/Registration**	**Enrolling**	**10**
X-linked Chronic Granulomatous Disease	**Kohn/UCLA**	**Phase 1/2**	**Enrolling**	**10**
X-linked SCID	**Sorrentino/St. Jude**	**Phase 1/2**	**Enrolling**	**12**
Sickle Cell Disease	**Kohn/UCLA**	**Phase 1**	**Enrolling**	**6**
Fetal alpha thalassemia major	**MacKenzie/UCSF**	**Phase 1**	**Enrolling**	**10**

Clinical Trials

HIV/AIDS Program Status

Indication	Investigator / Organization	Phase	Status	Targeted Enrollment
HIV	**Symonds / Calimmune**	**Phase 1/2a**	**Enrollment Complete**	**12**
HIV-Related Lymphoma	**Abedi / UC Davis**	**Phase 1**	**Enrolling**	**9-18**
HIV/AIDS	**Zaia / City of Hope**	**Phase 1**	**Enrolling**	**6-12**

Clinical Trials – Chemotherapy free conditioning in allogeneic X-SCID

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Investigator:
Judith Shizuru, MD, PhD

Institution: Stanford University

Rationale and Design

- *Monoclonal antibody that promotes engraftment of hematopoietic stem cells.*
- *Could replace toxic conditioning regimens and enable chemotherapy-free transplants*

Goal

- *Primary: Safety and feasibility*
- *Secondary: HSC engraftment and restoration of immune system*

Status

- *Enrolling*

Clinical Trials – ADA-SCID

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Investigator: Don Kohn, MD

Institution: UCLA & Orchard Biotherapeutics

Rationale and Design

- *Inherited genetic disease with primary immune deficiency due to Adenosine deaminase deficiency (ADA)*
- *Efficacy of chronic enzyme replacement therapy is uncertain in long-term*
- *Transplantation of gene corrected autologous blood forming stem cells*

Goal

- *Primary: Safety*
- *Secondary: Efficacy; gene marking; immune reconstitution*
- *Registration (BLA)*

Status

- *Orphan Drug Designation, Breakthrough Therapy, Rare Pediatric Disease Designation*
- *>40 patients have been treated including 9 patients in this on going clinical trial (9-15 mo.)*
- *Safety and initial efficacy data obtained*

CURED

Evie

Evangelina Padilla-Vaccaro

Diagnosed at birth with Severe Combined Immunodeficiency Disease

"Evie is my little genetically modified supergirl."

Alysia Vaccaro

Every Moment *Counts*

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Clinical Trials – X-CGD

Investigator: Don Kohn, MD

Institution: UCLA

Rationale and Design

- *Inherited primary immune deficiency*
- *Repeat bouts of severe, resistant infections*
- *Patients' own HSC gene modified*

Goal

- *Primary: Safety and efficacy*
- *Secondary: Restoration of immune function*

Status

- *Multicenter clinical trial with NIH, Boston Children*
- *Enrolled and treated 5 patients*
- *Early evidence of clinical efficacy*

CURED

Brenden Whittaker

Diagnosed with Severe Chronic Granulomatous Disease

"For people going through anything like this, don't give up. Keep fighting. Keep moving forward. Someday it will all work out."

Brenden W

Clinical Trials – X-SCID

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Investigators:
Brian Sorrentino, MD
Mort Cowan, MD

Institutions:
St. Jude Children's Hospital
UCSF

Rationale and Design

- Catastrophic immunodeficiency disorder caused by mutations in IL2RG gene
- Without a curative transplant-based therapy, X-SCID is lethal in typically in first year of life

Goal

- *Primary: Safety and feasibility*
- *Secondary: Efficacy; gene marking; immune reconstitution*

Status

- *Enrolled and treated 6 patients (including 2 patients at UCSF). (4-6 months)*
- *Evidence of restoration of functional immune system: both UCSF patients are at home and off isolation.*

Ronnie Priyank

X-SCID Trial

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Clinical Trials – Sickle Cell Disease

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Investigator: Don Kohn, MD

Institution: UCLA

Rationale and Design

- *Inherited mutation in hemoglobin gene causes red blood cells to "sickle", block small blood vessels*
- *Affects 100,000 in US*
- *Average lifespan –around 40 years*
- *Transplantation of patient's own gene modified blood-forming stem cells*

Goal

- *Primary: Safety, feasibility*
- *Secondary: Hematopoietic recovery; RBC function; Quality of life assessment*

Status

- *Enrolled and treated 1 patient*
- *Feasibility and early safety*
- *Example of value of Clinical Advisory Panel (CAP) in helping overcome technical challenges*
- *Partnered with Biomarin*

Clinical Trials – Fetal Alpha Thalassemia Major

Investigator:
Tippi MacKenzie, MD

Institution: UCSF

Rationale and Design

- *Alpha thalassemia major is fatal in utero*
- *Maternal to fetus hematopoietic stem cell (HSC) transplant may provide cure*
- *In utero HSC transplantation at 18-25 weeks*

Goal

- *Primary: Safety of maternal and fetal subjects*
- *Secondary: Feasibility; Efficacy (maternal/fetal HSC chimerism)*

Status

- *Award launched August 2017*
- *Patient recruitment initiating*

Clinical Trials – HIV

Investigator:
Geoff Symonds, PhD

Company: Calimmune

Rationale and Design

- No curative treatment for HIV
- Patient's own white blood cells and HSC are gene modified to create HIV-resistant blood/immune system

Goal

- *Primary: Safety and feasibility*
- *Secondary: Efficacy; gene marking/expression; viral load/T cell count*

Status

- *Enrolled and treated 12 patients*
- *Evidence of safety and feasibility*
- *CSL acquisition of Calimmune. Committed to complete CIRM funded clinical trial*

MISSION

CIRM's Mission

Accelerate stem cell treatments to patients with unmet medical needs.

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