Real Life™

Advancing Cell and Gene Therapies in California and Beyond

Lisa Kadyk, PhD and Lila R. Collins, PhD
Associate Directors, Therapeutics Development
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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

Created by Prop 71 and Continuing Under Prop 14

A Snapshot of Our Identity and Impact

2004

CIRM created by patient advocates and California stakeholders-Proposition 71

2020

Refunded under Proposition 14 - **$5.5B**

$1.5B earmarked for neurological diseases

1100+

Cutting edge research & translational programs funded

90 Clinical Trials, 3200+ Patients Enrolled

Mostly early stage; some close to seeking marketing approval

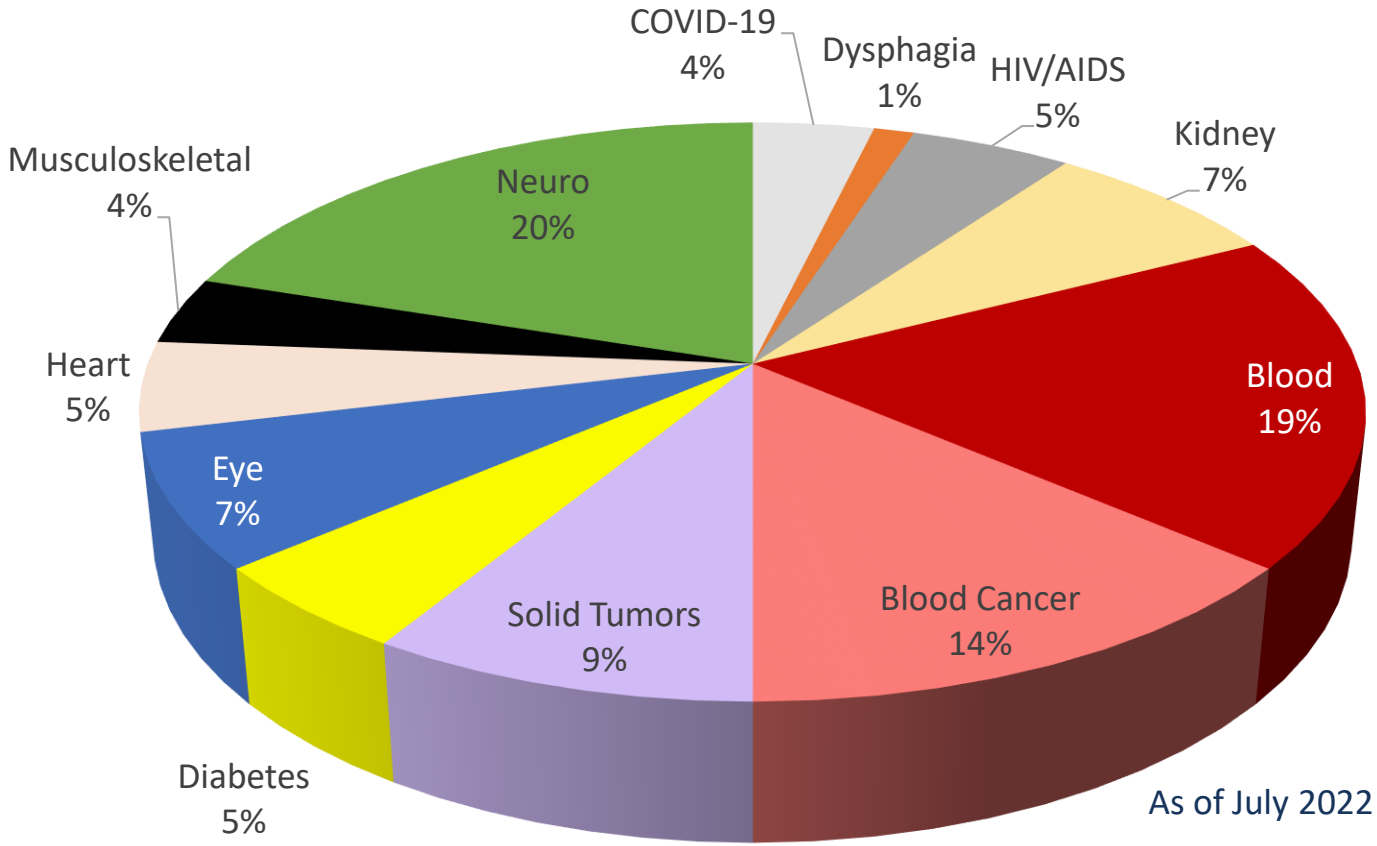
$23B

CIRM-funded projects raised over $23B in industry support

As of Dec 2022

Clinical Trial Portfolio To-Date

- **90** Clinical Trials funded through April 2023
- Wide Variety of Diseases and Disorders
- Different Approaches



Core Funding Opportunities

DISCOVERY

New Idea

DISC

$80M

2x a Year

TRANSLATION

Single Product Candidate

TRAN

$52M

2x a Year

CLINICAL

Pre-IND Meeting or Equivalent

CLIN1

CLIN2

Approved Therapy or Device

$162M

Monthly

FY 2022/23 Funding Allocation

DISC2 Funding Details

DISC2	Candidate	Funding Limit
Therapeutic	Stem Cell, Gene Therapy Biologic*, Small Molecule*	$1.5M
Diagnostic	Stem-cell based, *or*	$500K
Medical Device	Addresses a bottleneck for stem cell or gene therapies	$500K
Tool		$500K

Offered 2x/year

*Must act on a stem cell

TRAN Funding Details

	Aim / Scope	Eligibility	Funding Limit
TRAN 1	Therapeutic	Stem Cell, Gene Therapy Biologic* or Small Molecule* *Must act on a stem cell	$4M / $2M** ** $2M small molecule
TRAN 2	Diagnostic	Support Stem Cell, Gene Therapy or Combination	$1.2M
TRAN 3	Medical Device	Critical to Stem Cell, Gene Therapy or Combination	$2M
TRAN 4	Tool	Address Bottlenecks to Stem Cell, Gene Therapy or Combination	$1M

Offered 2x/year

CLIN1 and CLIN2 Funding Details

	Aim / Scope	Eligibility	Funding Limit
CLIN 1	IND Enabling	Pre-IND Meeting	Non-profit $6M For-profit $4M
CLIN 2	Clinical Trial	Active IND	Non-profit FIH* $12M, After FIH $15M For-profit FIH* $8M, After FIH $15M

*First in Human trial

- Monthly application deadlines
- Three months to funding (if successful).

Diversity, Equity and Inclusion

DEI principles are incorporated into all our initiatives

- Racial, ethnic, socio-economic, geographic diversity on research teams and for clinical trial participants
- Cultural sensitivity training for teams
- Active outreach programs for clinical trials
- Grant applications receive a “DEI” score in addition to a science score

CIRM Resources to Facilitate Success

Resources for Success: Advisory Panels

Convened for Clinical and Translational Awardees

Include Science/Clinical advisor and Patient Advocate

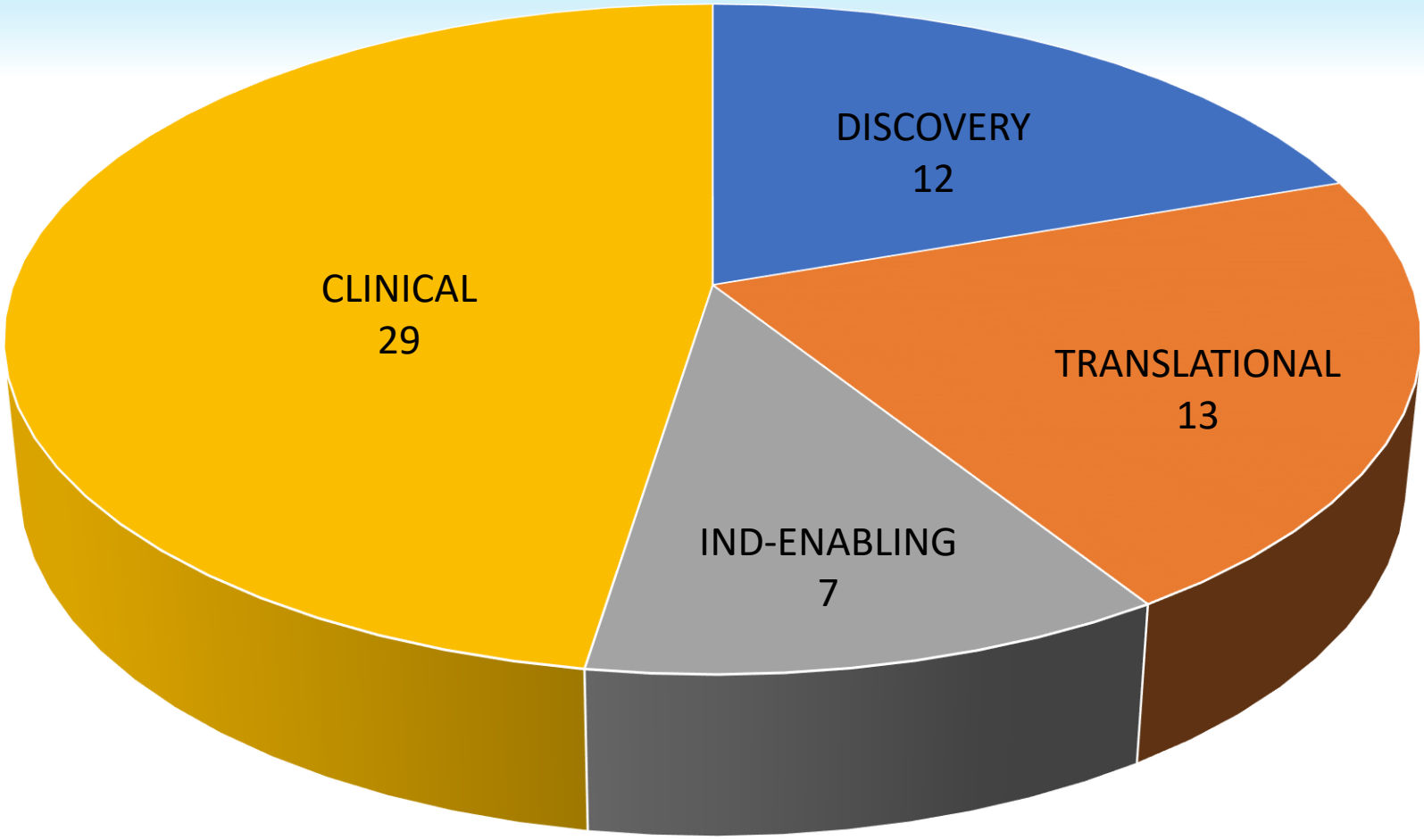
Discuss challenges and plan for success

Resources for Success: Alpha Clinics Network

- Accelerating cell and gene-therapy clinical trials
- Over 105 trials supported since 2015
  - 82 from industry sponsors
  - 23 CIRM-funded industry and academic sponsors
- $40M investment in patient-centered care and training (additional $80M budgeted for 2023)
- Over $100M in industry-contracts

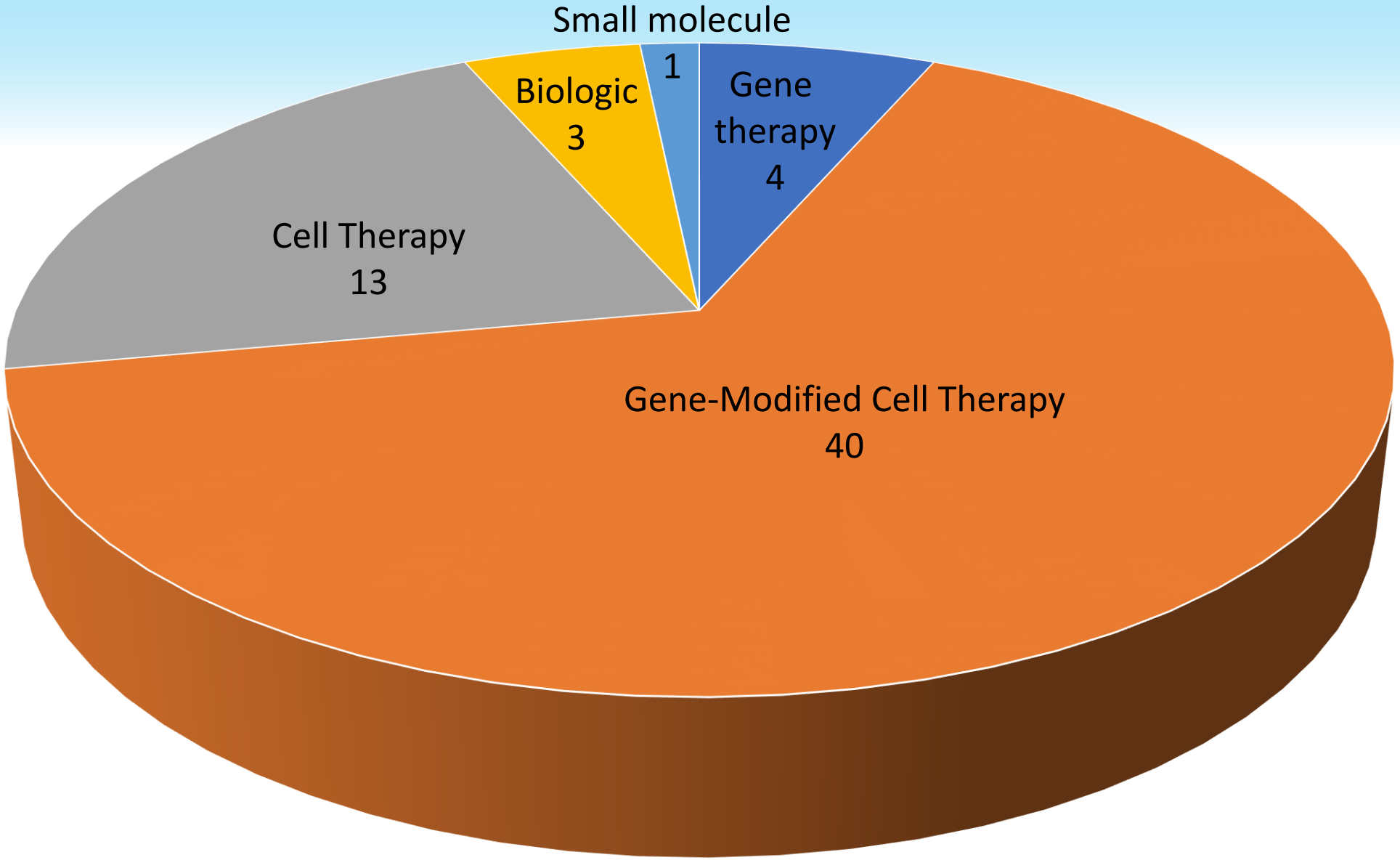
New Alpha Clinics added 2022: Stanford, Cedars-Sinai, USC

Active Awards Rare Disease Portfolio by Stage



61 total awards

Active Awards Rare Disease Portfolio by Approach



61 total awards

Clinical Portfolio: Cystinosis

Autologous transplant of adults with Cystinosis HSPC transduced with lentiviral vector encoding CTNS

Phase 1/2 Trial

PI: Dr. Stephanie Cherqui

Six patients treated

- Sustained engraftment
- Reduced cystine crystals in skin, intestinal mucosa
- Reduced or no requirement for oral medication

Partnered with AVROBIO for future development

Dr. Stephanie Cherqui

UC San Diego

Clinical Portfolio: Spina Bifida

In utero surgical repair with matrix seeded with placental MSC

Phase 1/2 Trial

PI: Dr. Diana Farmer

Preclinical efficacy

- Rescue of paralysis in sheep model
- Neuroprotective effect of MSC

Dr. Diana Farmer

Phase 1 completed

Six patients treated safely, in follow-up

Clinical Portfolio: Mucopolysaccharidosis Type I (MPSI)

Autologous transplant of B cells non-virally edited to produce α-L-IDUA

Phase 1 Trial

PI: Dr. Robert Hayes

- Sustained *in vivo* enzyme production
- Orphan Drug Designation
- Rare Pediatric Disease Designation

Trial launching

- Open-label, single-arm study in adults

Dr. Robert Hayes

IMMUSOFT

Clinical Portfolio: Leukocyte Adhesion Deficiency-I

Autologous transplant of children with LAD-I
HPSC transduced with LV vector expressing ITGB2 (CD18)

Phase 1/2 Trial
PI: Dr. Kinnari Patel

- Orphan Drug Designation

Dr. Kinnari Patel

Nine patients with >1 year follow-up (ASH 2022)

- CD18 expression restored in PMN cells
- 100% overall survival 12 months post GT
- Substantial reductions in infections and hospitalizations

Clinical Portfolio: Tay-Sachs Disease

Autologous transplant of patients with Tay-Sachs Disease HSPC transduced with LV vector expressing HexA/HexB

IND-enabling studies → IND filing
PI: Dr. Joseph Anderson

Dr. Joseph Anderson

- Tay-Sachs is a neurodegenerative disease, causing seizures, paralysis, blindness, deafness, shortened lifespan.

Therapeutic approach:

- Gene-corrected HSC reconstitute the immune system.
- HexA/HexB-expressing microglia in the brain deliver functional beta-hexosaminidase to affected neurons.

Translational Portfolio: Pitt-Hopkins Syndrome

Gene therapy for patients with Pitt-Hopkins Syndrome
AAV9 vector expressing TCF4

IND-enabling studies → IND filing
PI: Dr. Allyson Berent

- PHS is a rare neurodevelopmental disorder causing absence of speech, delayed development, seizures
- No treatment available

Therapeutic Approach:
- Single intracerebral microinjection of AAV9-TCF4


Dr. Allyson Berent

MAHZI therapeutics

Thank You!

lkadyk@cirm.ca.gov

lcollins@cirm.ca.gov

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