Right now.

President's Report

May 23, 2019

Maria T. Millan, M.D.

President and Chief Executive Officer
California Institute for Regenerative Medicine

CIRM
CALIFORNIA'S STEM CELL AGENCY

2004

$3B Bond funding -Proposition 71

1000

Projects Funded

53

Clinical Trials

1200

Patients Enrolled

SOMETHING BETTER THAN HOPE

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Every Moment Counts. **Don't Stop** Now.

Status of CIRM 5-year Strategic Plan

2019
Year 4 Mid-Year Update

DISCOVER 50 NEW CANDIDATES

2019 YTD: *pending*

New Candidates

TOTAL: 36

ADVANCE THROUGH DEVELOPMENT

2019 YTD: **3**

Progression Events

TOTAL: 61

(110% increase)

REFINE REGULATORY PATHWAY

2019 YTD: *pending*

RMAT

TOTAL: 5

SHORTEN TIME TO CLINICAL TESTING

2019 YTD: *pending*

IND in 18 months

TOTAL: 4

(Average time to IND: 20.4 mo. for 8 CLIN1)

EXPAND 50 NEW TRIALS IN 5 YEARS

2019 YTD: **3**

New Trials

TOTAL: 36

(total 53 trials)

INCREASE INDUSTRY PULL

2019 YTD: **3**

Partner Events

TOTAL: 30

(50% CLIN programs partnered)

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CIRM Investments

INFRASTRUCTURE	EDUCATION	DISCOVERY	TRANSLATION	CLINICAL
$482M	$219M	$905M	$329M	$684M

$2.6B and 1000 Awards

$1.3B for Therapeutic Research & Development

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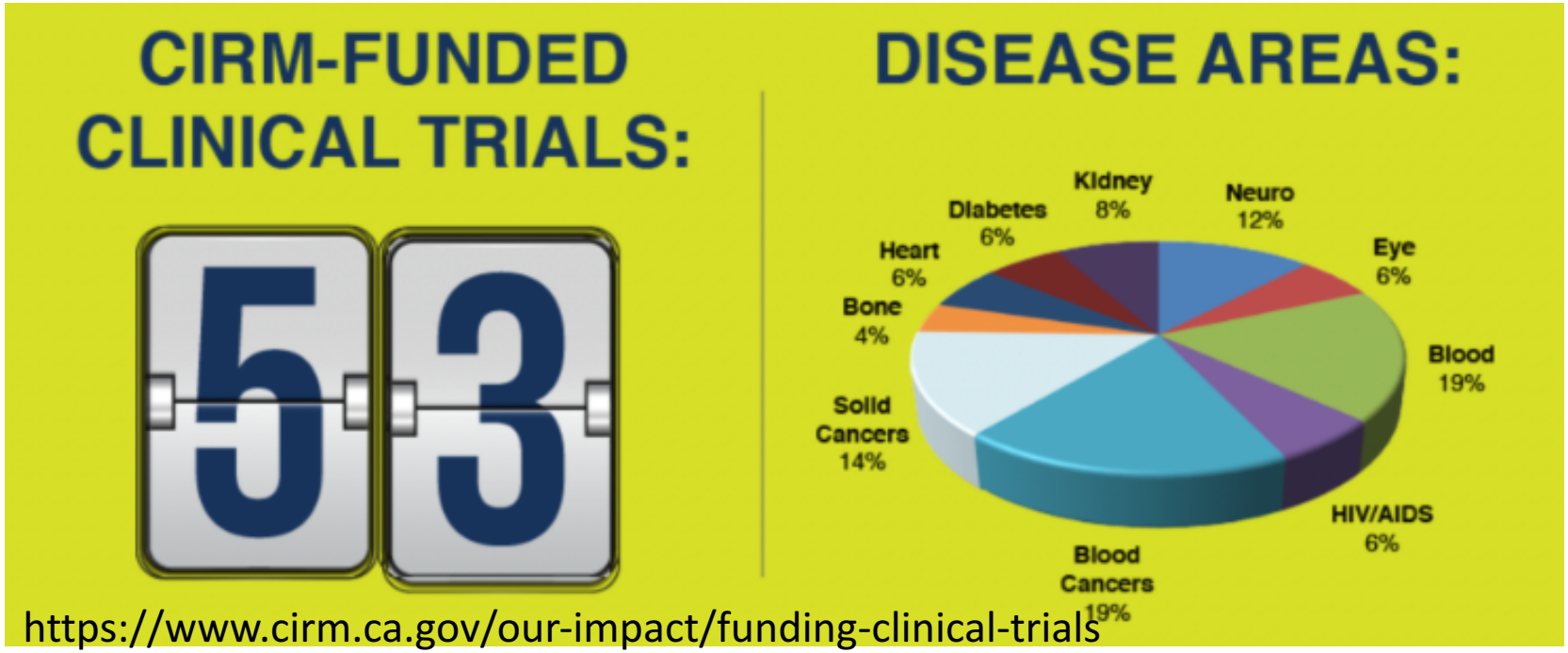
CIRM Clinical Trials



https://www.cirm.ca.gov/our-impact/funding-clinical-trials

- 36 New trials since 2016 Strategic Plan
- 42 Open trials
- 8 Completed trials
- 3 Terminated

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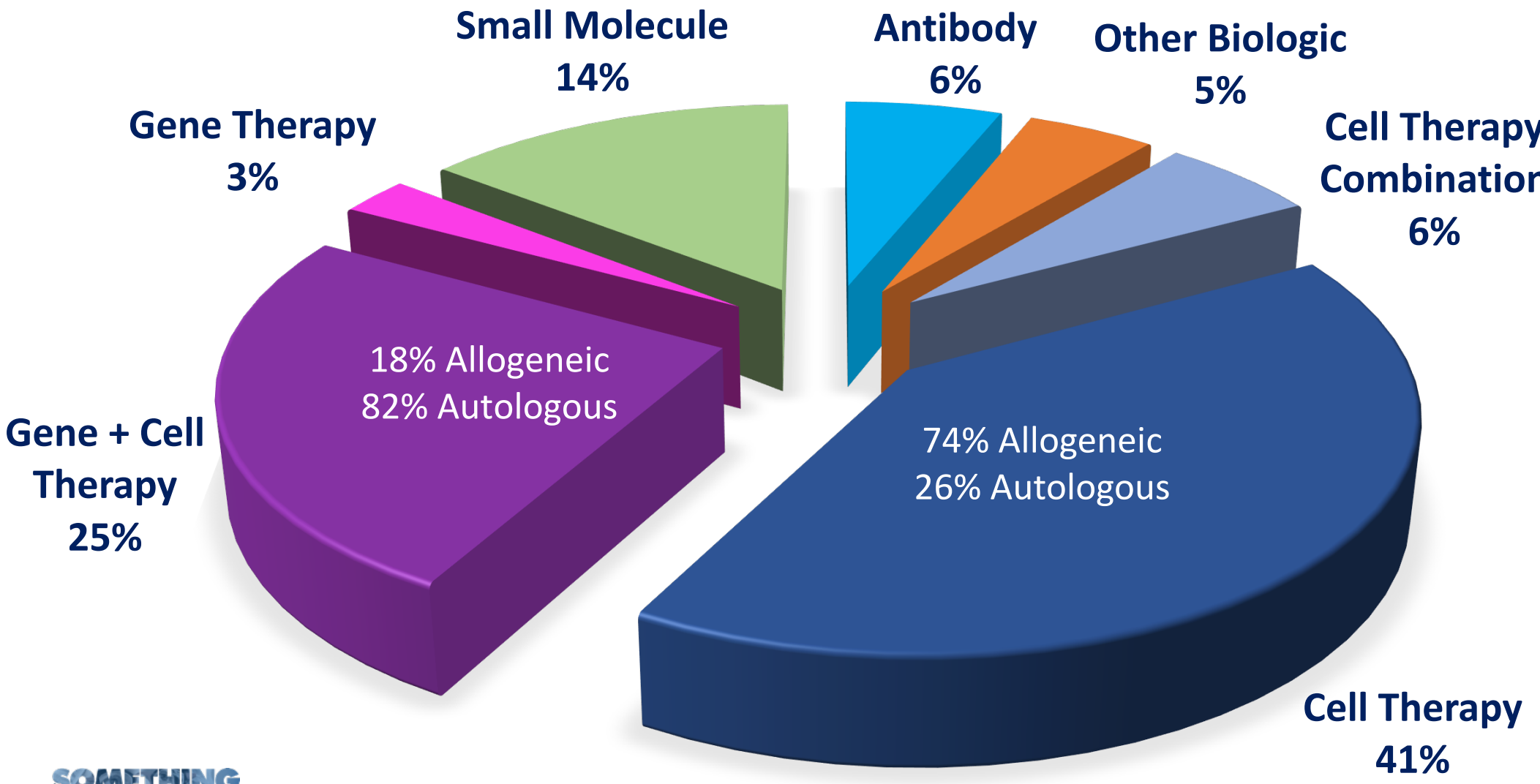
CIRM's unique focus on Cell and Gene Technology



N = 264 Therapeutic Discovery/Development Awards , $1.27 B

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CIRM Clinical Portfolio: Next Generation CAR-T

Phase 1 open label dose escalation multicenter trial to test CAR-T for relapsed/refractory Multiple Myeloma (n=40)

- CAR-T Product engineered via non-viral vector
- gene targeting myeloma selective protein BCMA
- Purified for CAR-T cell TSCM (stem cell memory T cells) - persistence & to decrease exhaustion
- Rimiducid-reactive “safety switch”

POSEIDA THERAPEUTICS

FDA RMAT expedited pathway designation

$19.8M CIRM funding

Recent Series C financing of $142M ($75M Equity Investment from Novartis)

CIRM Clinical Portfolio: ADA Severe Combined Immunodeficiency

Autologous transplant of children with ADA SCID
CD34+ HSC transduced with LV encoding human ADA

Phase 2 Registration Trial
$19M CIRM funding
PI: Don Kohn

UCLA Orchard therapeutics

20 patients with 2 yr. follow up (Feb 2019 report):

- 100% event-free survival at 24 months
- Favorable outcomes compared to historical BMT registry groups

BLA planned for 2020

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CIRM Clinical Portfolio: X-linked SCID

Autologous gene modified bone marrow stem cell transplant of infants with X- SCID after busulfan conditioning

LV delivery of normal copy of gene for IL2RG chain

Phase 1/2 trial: 28 participants St. Jude/UCSF

PI: Stephen Gottschalk

$11.9M CIRM funding

Licensed by Mustang Bio

Photo of Dr. Brian Sorrentino, In memory. From ASH

8 infants with 16 month median follow-up with multi-lineage engraftment, functional T and B Cells and normal NK counts. NEJM April 18, 2019

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CIRM Clinical Portfolio: X-linked Chronic Granulomatous Disease

A Phase I/II, Non Randomized, Multicenter, Open-Label Study of G1XCGD (Lentiviral Vector Transduced CD34+ Cells) in Patients With X-Linked Chronic Granulomatous Disease

$7M CIRM funding for the Phase 1/2 Clinical Trial

10 participants

PI: Don Kohn UCLA

Partnered with Orchard Therapeutics

Clinical proof of concept data Six patients with sustained levels of functioning neutrophils 12 months after treatment with gene therapy and no longer receive CGD-related prophylactic (ASH Dec. 2018)

CIRM Clinical Portfolio: Improving Transplant Approaches for SCID

Phase I trial : *A monoclonal antibody that depletes blood stem cells and enables chemotherapy-free transplants*; 24 patient trial

PI: Judith A. Shizuru, Stanford

Stanford MEDICINE

$19M Dis. Team funding (IND-enabling + Phase 1)
$3.7M CLIN2 (to complete Phase 1)
$2.3M Co-funding

Goal: Replace SCID patients' dysfunctional immune cells with healthy ones using an antibody instead of toxic chemotherapy as a safer form of bone marrow transplant.

Interim data:

- Safe and well tolerated thus far
- 3 of 5 patients have clear evidence of blood stem cell engraftment
- Patients that had no B-cells before now have B-cells
- Indications of blood stem cell engraftment that gave rise to new myeloid and lymphoid cells
- Data for 6 patients being prepared for publication

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CIRM Clinical Portfolio: Beta Thalassemia

Phase 1/2 study with the most severe form β^0/β^0; 6 patient trial. Autologous transplant with Zinc finger nuclease gene edited HSC to upregulate fetal Hgb

PI: Weston Miller, Sangamo

Sangamo THERAPEUTICS

SANOFI

Bioverativ

$8M CIRM funding

Interim data:

- Engraftment of gene edited cells in 1st enrolled patient
- Gene edited cells in circulation
- Neutrophil and platelet recovery, within two and four weeks of infusion
- Stable hemoglobin for 7 weeks with rise in fetal Hgb levels from 1% to 31%
- Transfusion independent from weeks 3-7 after treatment

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CIRM Clinical Portfolio: Sickle Cell Disease

- CIRM and NHLBI MOU to jointly fund industry and academic cell and gene programs for the Cure Sickle Cell Initiative
- Leverages CIRM's Processes and Funding Infrastructure
- American Society of Hematology setting up registry & data capacity

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CIRM Clinical Portfolio: Sickle Cell Disease

- 100,000 in the U.S. & millions worldwide- pain crises, multi-organ damage, recurrent hospitalization
- Average lifespan in U.S. ~ 40 years
- Life span <5yrs. for SCD infants in sub-Saharan Africa; 30% growth in those affected globally by 2050

Walters (CHORI) CURE SICKLE CELL.	**CRISPR/Cas9 gene correction Just Progressed to CLIN1 stage** **CIRM-NHLBI co-funding** **TRAN $4.5M; CLIN1 $4.5M (portion by NHLBI)**
Kohn (UCLA)	Phase 1 LV gene addition (anti-sickling globin protein) **CLIN2 $13M; 6 patients**
Rosenthal (City of Hope)	**Phase 1 mild conditioning** **for haplo-match BMT** **CLIN2 $5.7M; 6 patients**
Porteus (Stanford)	**IND-enabling CRISPR/Cas 9 gene editing (Val to Glu)** **CLIN1 $4.9M**

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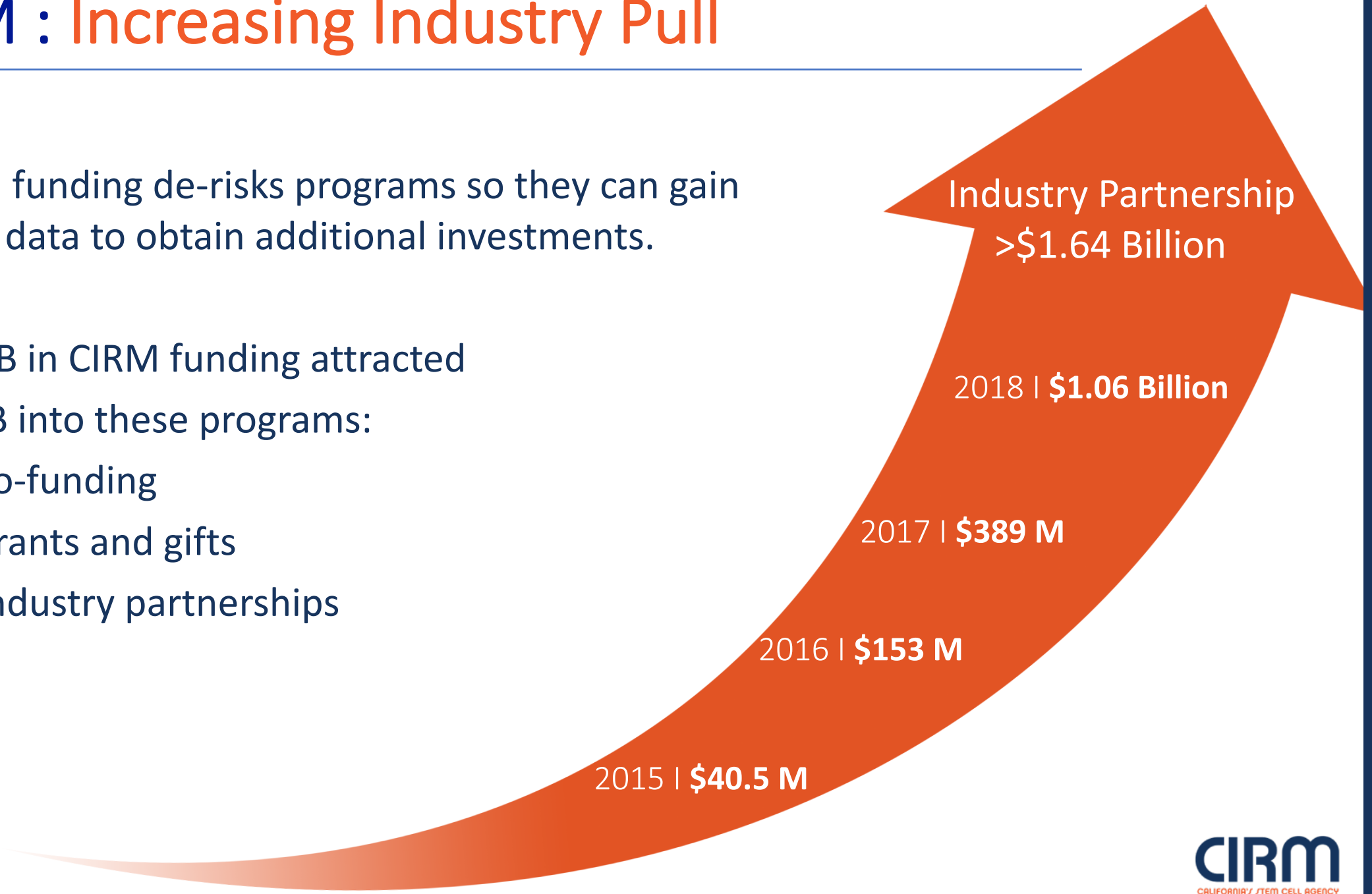
CIRM : Increasing Industry Pull

CIRM funding de-risks programs so they can gain early data to obtain additional investments.

$2.6 B in CIRM funding attracted

$3.2B into these programs:

- co-funding
- grants and gifts
- Industry partnerships



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CIRM : A Hub to Promote Partnership

Credit for image: Scihub Copernicus

Hub for Interactions with and between grantees, non-profit Organizations, the Public & Industry

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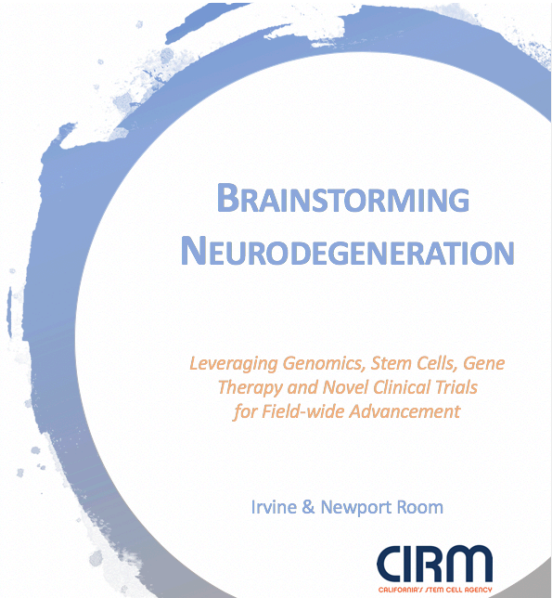
CIRM: Convene, Connect, Promote Knowledge Transfer

Annual Meetings- Alpha Clinics Symposium, Bridges, SPARK



Workshops

GForce-PD
A Global Effort to Bring Cell Based Therapies to PD Patients

Consortia & other initiatives spin-off from CIRM meetings and workshops

Publications

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Retaining Talent and Expertise

Upcoming Presentations from CIRM Team & Research Program Highlight:

- Retired Annuitants: Request from CIRM to maintain uninterrupted continuity of expertise and knowledge from our retirees. Scott Tocher (Action)

- CIRM 2019-2020 Budget Proposal: Supporting the transition plan/ wind-down of Prop 71 funding and the interim to a possible 2020 Bond Initiative. Chila Silva-Martin (Action)

- CLIN programs for ICOC consideration. Shyam Patel (Action)

- Clinical Highlight: How a CIRM funded program was translated to the clinics, partnered with industry and progressing to address unmet medical needs Mark Chao, 47 Inc. (Update)