Real Life™

Strategic Progress and Priorities of CIRM

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President & CEO
CFAOC Meeting
November 9, 2022

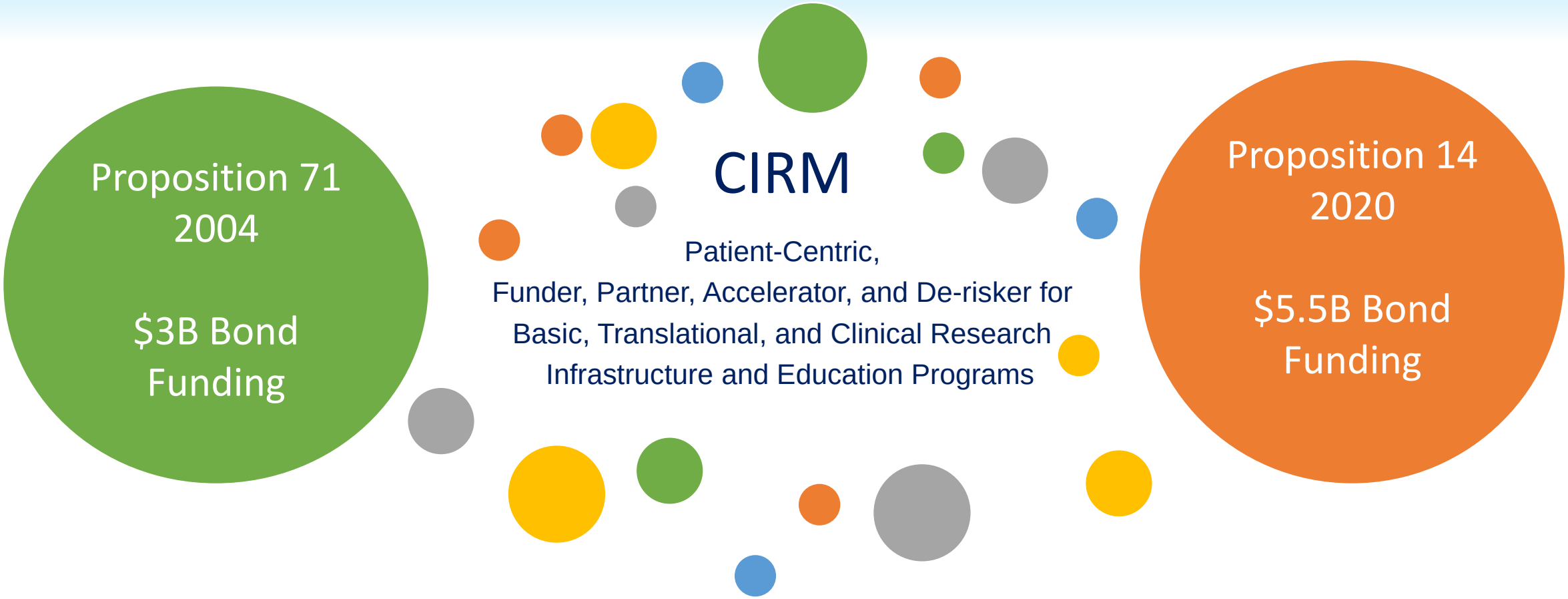
CIRM
CALIFORNIA'S STEM CELL AGENCY

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



Advancing World Class Science through Funding Pillars

Strategic Plan Development & Launch

	Prop 71 Era	Transition Months Nov 2020-Jan 2021	Prop 14 Era
Discovery	574	11	58*
Translation	97		18
Clinical	95	4	18*
Education	207		73
Infrastructure	49		5 Supplemental Awards

Data as of: Sep 2022

*Include DISC and CLIN awards funded with Prop 71 money

CIRM's Pillar Programs & Investments

$3.6B in total grants to date

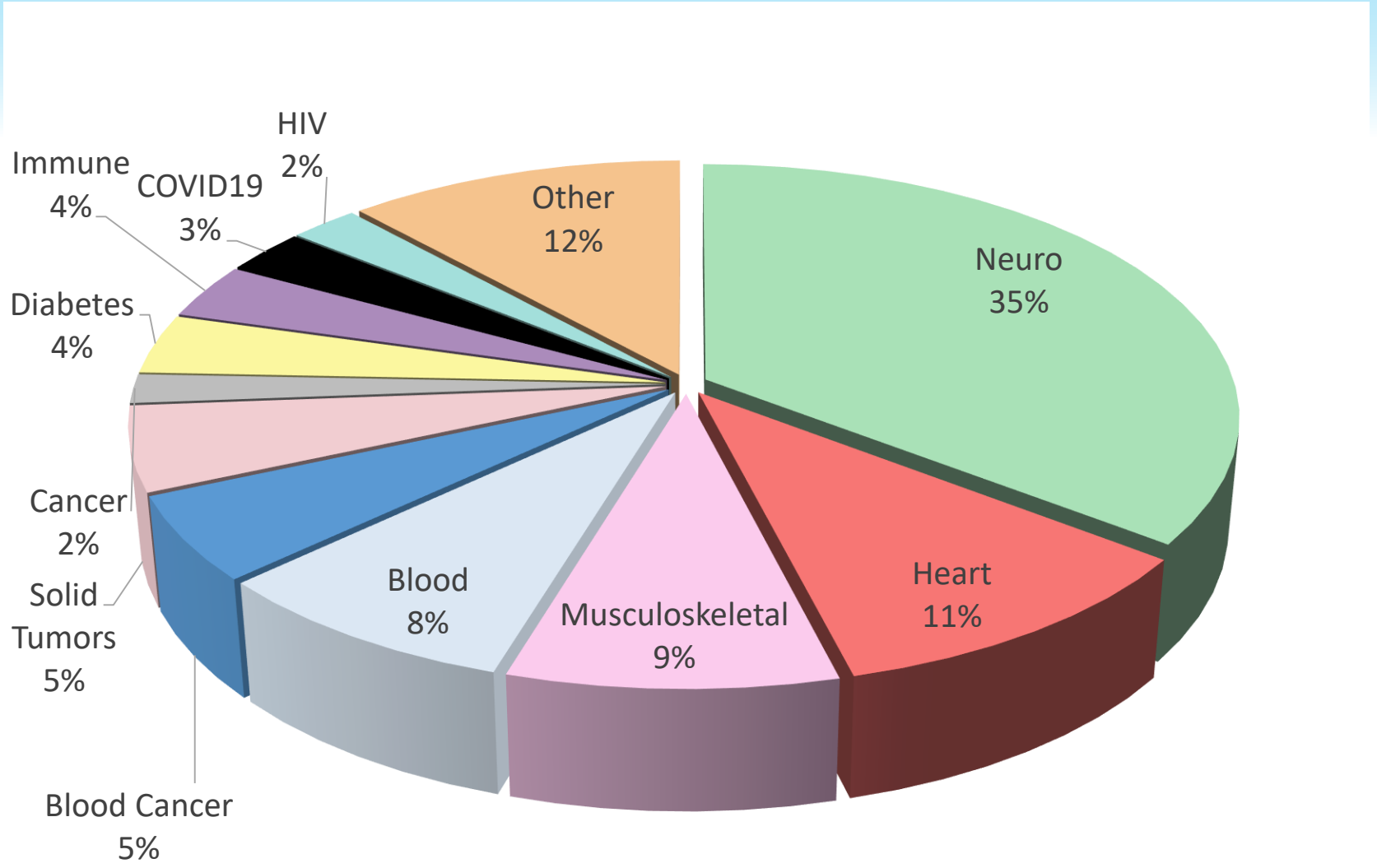
	DISCOVERY	TRANSLATION	CLINICAL	EDUCATION	INFRASTRUCTURE
	$1.1B	**$503M**	**$1.1B**	**$430M**	**$489M**
Prop 14 era	**$75M***	**$77M**	**$147M***	**$190M**	**$3M**

*** 23** awards equating to **$88M** in the neuro space in Prop 14 era

Data as of: Sep 2022

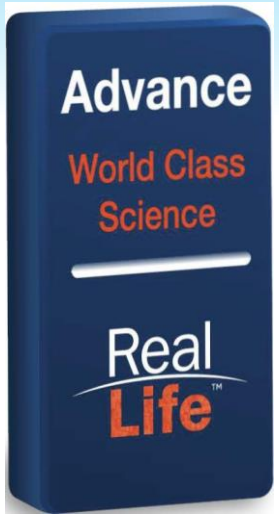
*Include DISC and CLIN awards funded with Prop 71 money

CIRM's Investment in Diverse Disease Etiologies



Data as of: Sep 2022
% normalized to total R&D awards

Prop 14-Era: Our 5-Year Strategic Plan



- Develop shared resources
- 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

A commitment to diversity, equity, and inclusion

Cell-Gene Therapy for Immune Diseases All with Accelerated FDA Designations

Don Kohn ***UCLA/Orchard Therapeutics***	**ADA-SCID**	• Durable restoration of immune system • Cures at 24 months in 50 patients (median age 9 months)	 *Evie*
Stephen Gottschalk *St. Jude/UCSF/ Mustang Bio*	**X-SCID**	• 8 patients w/ 16 mo. Median follow up • Normal T cell and NK counts achieved at 4 months- becoming normal	 *Ronnie*  *Ja'Ceon*
Mort Cowan & Jennifer Puck *UCSF*	**ART-SCID**	• Promising, with 13 patients • Clinical trial is active and enrolling	 *Hataali*
Kinnari Patel *Rocket Pharma*	**Severe LAD-1**	• Engraftment in all 9 severe LAD-I patients • Restoration of the key antigen CD18 expression leading to decreased infections	*Marley* 

CIRM Partnership Advances Therapies for Rare Diseases

Principal Investigator/ Institution	*Ex Vivo* Cell-Gene Therapy Approach	Pre-Clinical	Early-Stage Clinical (Phase 1 and 2)	Late-Stage Clinical (Phase 3)
Matthew Porteus *Stanford University*	Gene Correction of mutation (AAV6 delivery) CRISPR/Cas9	CIRM	*Phase 1* *Graphite Bio*	
Donald Kohn *UCLA*	Genetic modification (Lentiviral delivery) Anti-sickling globin	CIRM	*Phase 1* CIRM	Evie Jr James
Mark Walters *UCSF Benioff Children's Oakland*	Gene Correction of mutation (non-viral delivery) CRISPR/Cas9	CIRM	 *CIRM –NIH partnership* *Phase 1*	
David Williams *Boston Children's Hospital*	Fetal hemoglobin prevents sickling but is silenced post-natally. shRNA to BCL11a (repressor fetal hemoglobin expression)	NIH National Institutes of Health	*CIRM –NIH partnership* *Phase 1/2* 	

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

- Spina Bifida happens when the neural tube doesn't close all the way, often resulting in damage to the spinal cord and nerves and paralysis.

CuRe Trial:
Placental stem cells on amniotic membrane patch (approved) for dura replacement – pilot study with 6 patients

Encouraging, preliminary results
3 babies have been born and are being monitored for 6 years with a key checkup at 30 months

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

Baby Robbie at 15 days and mom, Emily

DEI Tracking in our Clinical Programs

	Black	Hispanic	White (Non-Hispanic)	Multi Racial	American Indian/ Alaskan Native	Asian	Native Hawaiian/PI
California census	7%	39%	37%	4%	2%	16%	1%
3004 subjects enrolled in 61 CIRM clinical trials*	**9%**	**14%**	**58%**	**1%**	**1%**	**5%**	**0%**
US census	13%	19%	60%	3%	1%	6%	<1%

*As of Q1 2021
2% "other"
9% "unkown"
**Including cancer, neurodegenerative disease, and rare disease (Also as of Q1 2021)

DEI Enhancements to CIRM Clinical Programs:

- DEI milestone incorporated in the Grant Notice of Award to hold the Awardee accountable for their proposed DEI plan
- Monitor DEI Plan implementation and progress through Quarterly Reports and Clinical Advisory Panels
- Improve tracking of demographics along with disease indications and expanded categories, including social determinants, in accordance with best practices and evolving descriptors and guidelines (e.g. State of California, National Academies, NIH)

DEI Review Criteria for Board Members

Basis for DEI Score on Clinical Applications

1. Commitment to DEI: How well the project team demonstrates a commitment to developing a therapy that will ultimately serve the unmet medical needs of the diverse California population, including underserved and disproportionately affected populations. Teams are asked to describe disparities that may impact populations that would ultimately utilize their product, set reasonable trial enrollment targets, and allocate appropriate resources to meeting DEI goals within their project.

2. Project Plans: How well the project team plans for and proposes activities that are likely to achieve inclusive outreach, engagement, enrollment, and retention of trial participants from underserved or disproportionately affected populations.

3. Cultural Sensitivity: How well the proposal addresses and will increase cultural sensitivity on the project team and at partner institutions.

CIRM CLIN Program DEI Rubric

CRITERIA	Score of 0 to 2 Not Responsive	Score of 3 to 5 Not Fully Responsive	Score of 6 to 8 Responsive	Score of 9 to 10 Outstanding Response
1. Commitment to DEI	Fails to address how success of this project would lead to a therapy that positively impacts underserved or disproportionately affected communities.	Inadequately addresses how success of this project would lead to a therapy that positively impacts underserved or disproportionately affected communities.	Adequately describes how success of this project would likely lead to a therapy that positively impacts underserved or disproportionately affected communities.	Convincingly and clearly describes how success of this project would lead to a therapy that positively impacts underserved or disproportionately affected communities.
	Does not set goals for diverse trial population enrollment and provides no justification for the target enrollment.	May set trial population enrollment goals that are inappropriate or infeasible relative to the population affected or at risk for the indication.	Sets adequate goals for trial population enrollment relative to the population affected or at risk for the indication.	Trial population goals are based on a deep understanding of health disparities and disease burden.
	Inadequate personnel/expertise or budget to implement DEI-oriented activities.	May have inadequate personnel/expertise or budget to implement DEI-oriented activities.	Adequate personnel/expertise or budget to implement DEI-oriented activities.	Strong personnel/expertise and appropriate budget to implement DEI-oriented activities.
2. Project Plans	Planned activities do not reflect a good faith effort and are unlikely to be effective in outreach and engagement.	Planned activities are incomplete or inadequate and may not reflect a good faith effort for outreach and engagement.	Planned activities reflect a good faith effort and have the potential to be effective in outreach and engagement.	Planned activities reflect an outstanding and comprehensive effort for outreach and engagement.
	Does not demonstrate an understanding of the potential barriers to participation in the clinical trial.	Does not fully demonstrate an understanding of the potential barriers to participation in the clinical trial.	Demonstrates an understanding of the potential barriers to participation in the clinical trial.	Demonstrates a clear understanding of the potential barriers to participation in the clinical trial.
	Inadequate plan to address potential barriers to participation.	May not have an adequate plan to address potential barriers to participation.	Has an adequate plan to address potential barriers to participation.	Has a strong plan to address potential barriers to participation.
	Unlikely to achieve the recruitment of trial participants from underserved or disproportionately affected populations.	May not be able to achieve the recruitment of trial participants from underserved or disproportionately affected populations.	Likely to achieve the recruitment of trial participants from underserved or disproportionately affected populations.	Very likely to achieve the recruitment of trial participants from underserved or disproportionately affected populations.
3. Cultural Sensitivity	Does not include activities to increase cultural sensitivity on the team or at partner institutions, or activities proposed are not appropriate.	Proposed activities may not be effective or sufficient to increase cultural sensitivity on the team or at partner institutions. Activities may not match the needs of the project.	Has appropriate plans to increase cultural sensitivity on the team or at partner institutions. Activities match the needs of the project.	Outstanding plans to increase cultural sensitivity on the team or at partner institutions. Activities are well matched to the needs of the project.

DEI Score: 0-10 scale

Our Key Mechanisms for Advancement of Therapies: Current Programs and Future Priorities

1) De-risking programs
2) Serving as a reliable resource for both non-profit and for-profit sectors (especially in volatile financial climates)
3) Bridging the valley of death
4) Creating a manufacturing network
5) Providing a network of top California medical centers to deliver CGT clinical trials to patients through partnerships
6) Expanding the access of clinical programs to ensure diversity, equity and inclusion

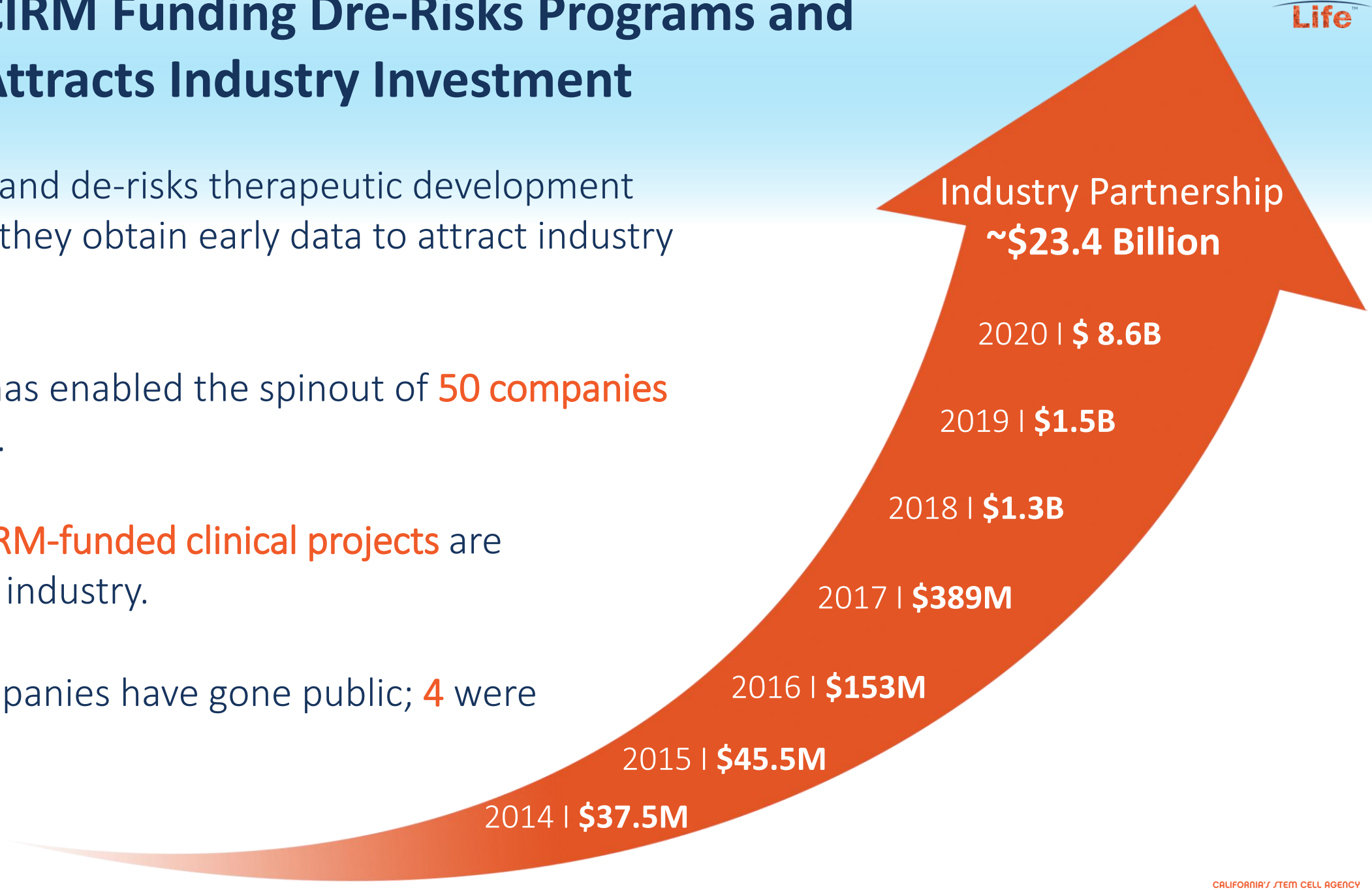
CIRM Funding Dre-Risks Programs and Attracts Industry Investment

CIRM nurtures and de-risks therapeutic development programs until they obtain early data to attract industry partnerships.

CIRM funding has enabled the spinout of 50 companies from academia.

Over 50% of CIRM-funded clinical projects are partnered with industry.

6 portfolio companies have gone public; 4 were acquired



CIRM Funding Bridges the Valley of Death

In Utero Cell Therapy

New Idea → Single Product Candidate → Pre-IND Meeting → IND → Ph 1 → Ph 2 → Ph 3 → Approved Therapy

1 TRAN Award **1 CLIN1 Award** **1 CLIN2 Award**

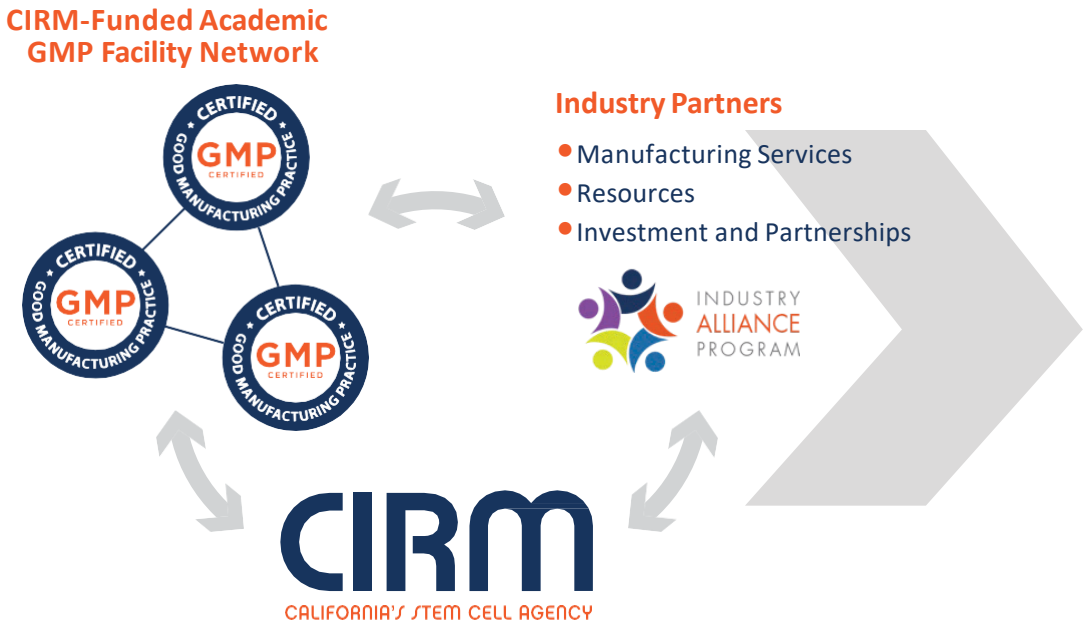
Cell Therapy for Retinitis Pigmentosa

New Idea → Single Product Candidate → Pre-IND Meeting → IND → Ph 1 → Ph 2 → Ph 3 → Approved Therapy

1 DISC Award **1 TRAN Award** **3 CLIN2 Awards**

In Development: CIRM Manufacturing Network

Goal: To overcome manufacturing hurdles for the delivery of regenerative medicine therapies by building a public-private manufacturing partnership network

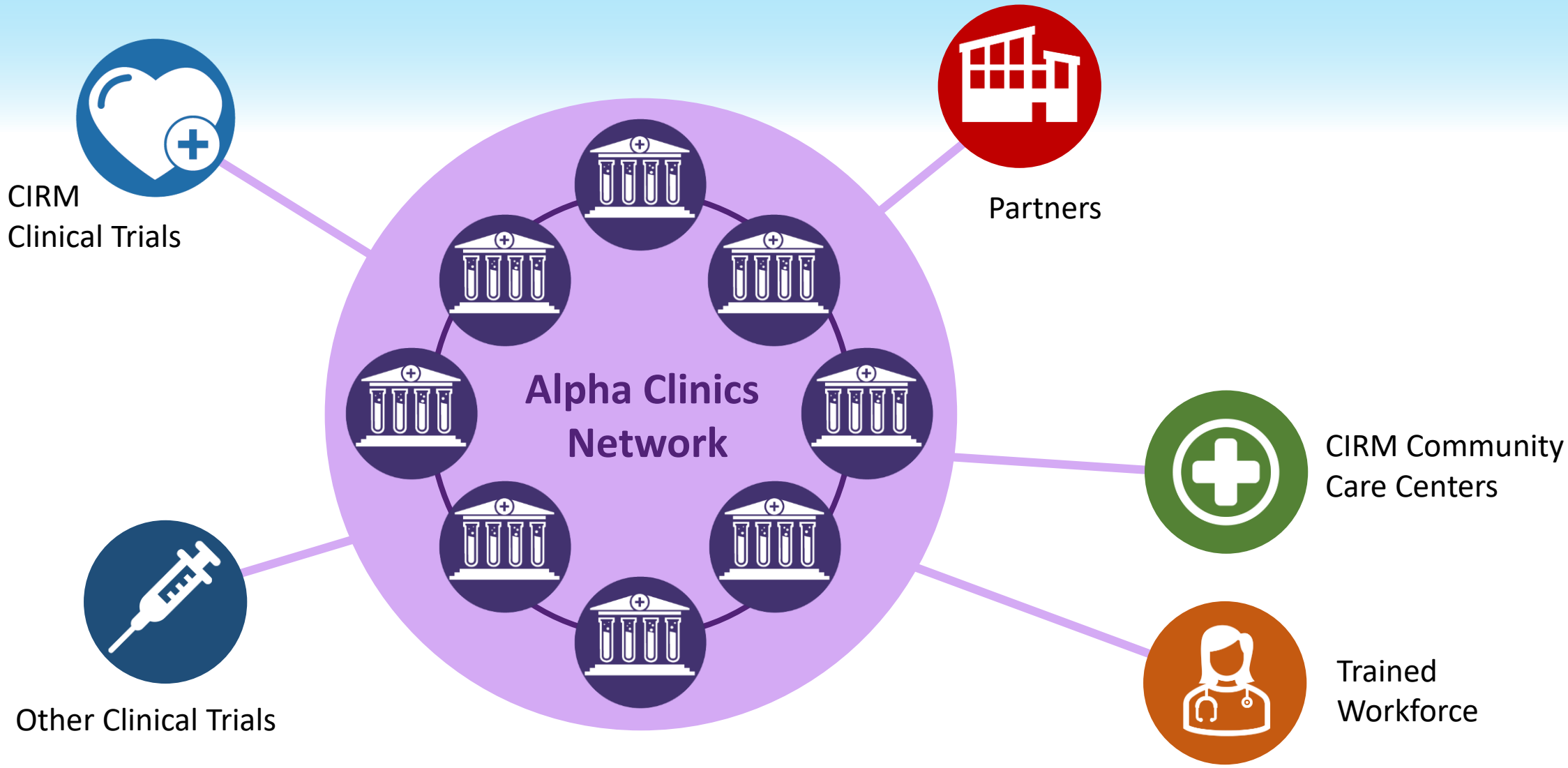


- **Accelerate** and de-risk path to commercialization
- **Advance** standards and quality by design
- **Build** manufacturing leadership and workforce

Alpha Clinics Network: Making Clinical Trials Accessible to Many

- Currently supporting 6 Alpha Clinics sites and recently funded 3 additional one
- $100M investment in patient-centered care and training, to-date
- Successfully accelerating cell and gene-therapy clinical trials
- Over 200 trials supported since 2015
- Over $100M in industry-contracts

A Robust Competency Hub



CIRM's Training Programs Train the Future Workforce

SPARK/EDUC3

HIGH SCHOOL

530 alumni
(9 summers, $4M)
2012-2021
~80% in college or beyond

Bridges/EDUC2

UNDERGRAD/MASTERS

1707 alumni
(13 years, $93M)
2009-present
65% of alumni are employed; 62% in science-related fields

Research Training/EDUC4

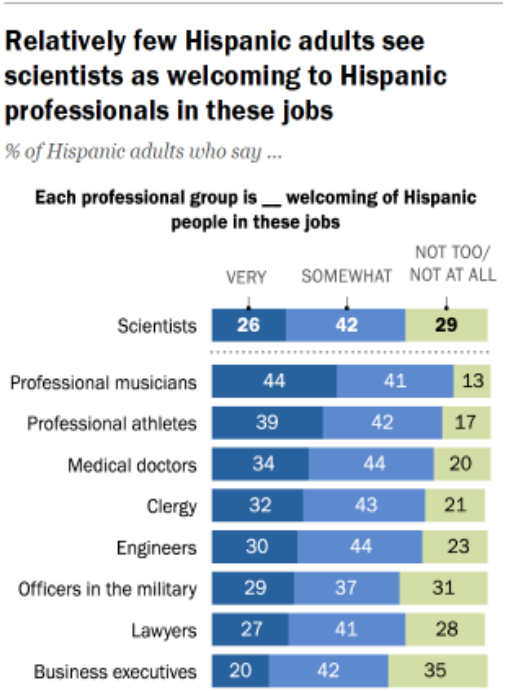
PRE/POSTDOCTORAL and MD

940 alumni
(11 years, $117M)
2006-2017
56% continued to further training

Distrust Feeds Disparity in Science and Medicine

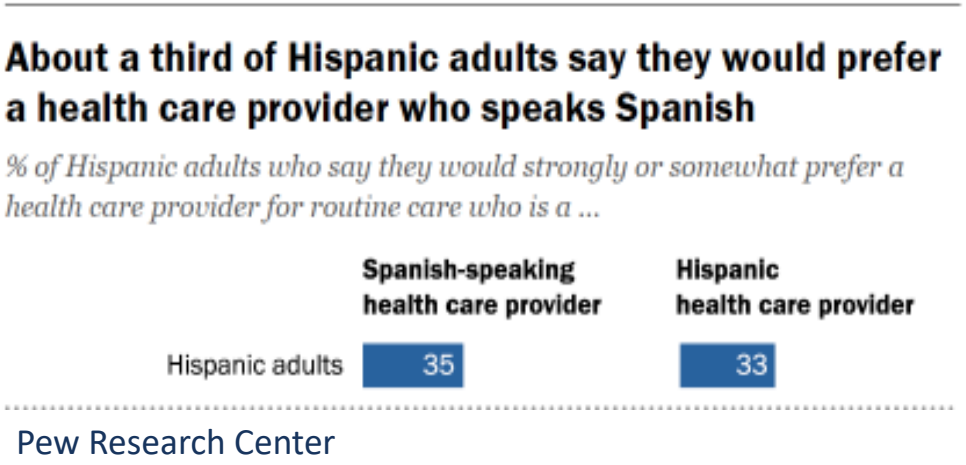
Hispanic workers make up 17% of total employment across all occupations, but just **8%** of all STEM workers.

(Pew Research Center analysis of federal government data)



Pew Research Center

Patients are most likely to participate in a trial when asked by a trusted provider (Woodcock et al. NEJM 2021)

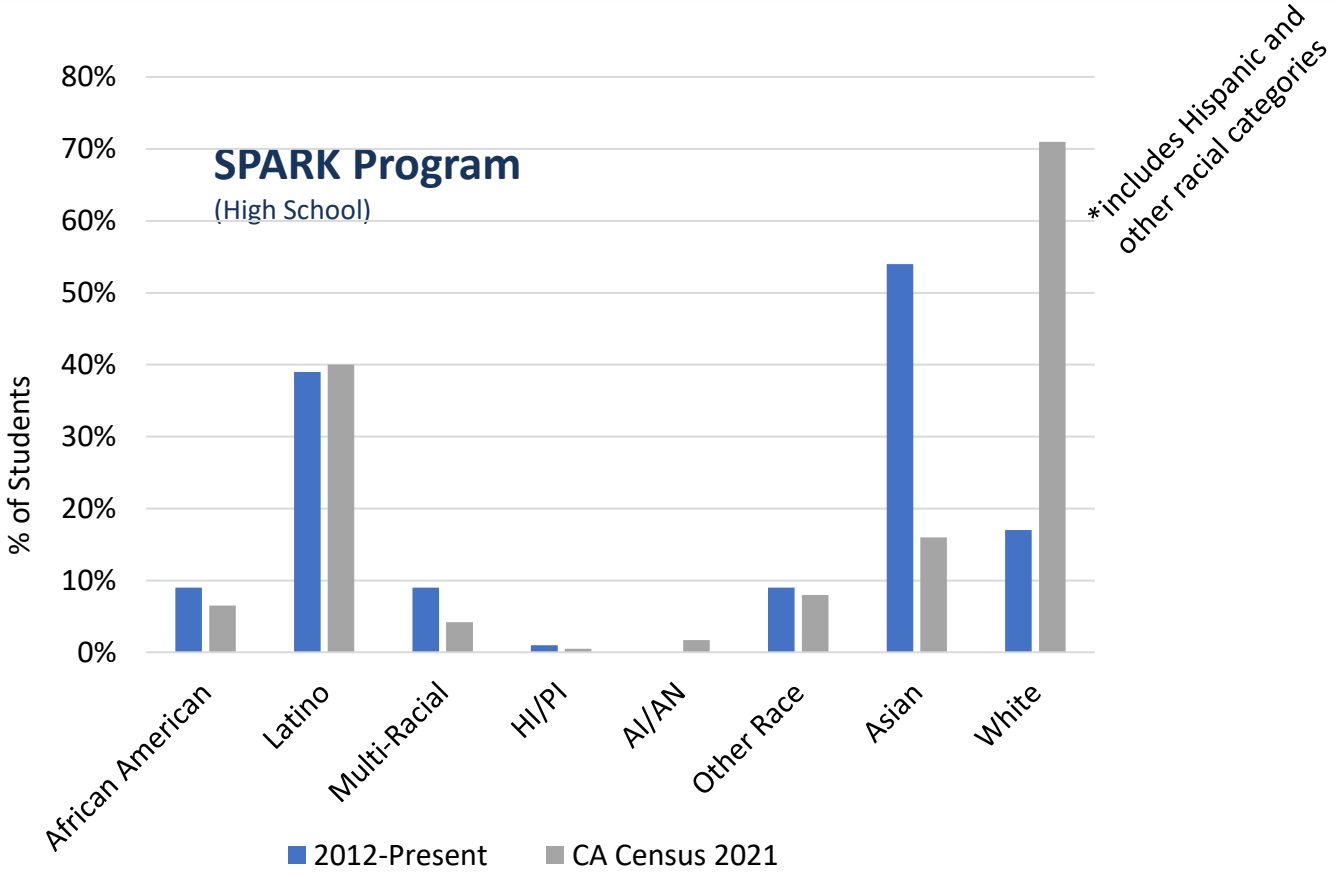


Pew Research Center

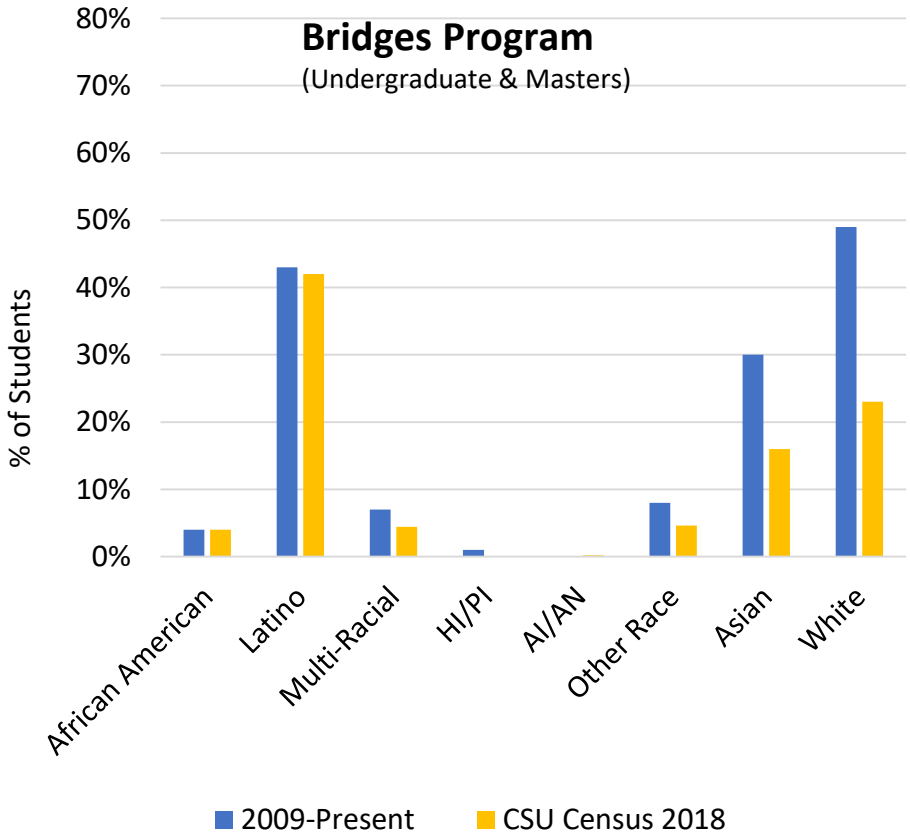
Goal: Foster a culturally competent and diverse scientific and medical workforce

Fostering Diversity in Science through Education

CIRM Education programs under Prop 71 were designed to "broaden participation of individuals representing the diversity of California" including those who "may not have had opportunities" and are "hindered by socioeconomic constraints."



N for Race = 454
N for Ethnicity = 307



N for Race = 1587
N for Ethnicity = 994

A Snapshot of Two Successful Alumni

Keau Wong, MBT

CSU San Marcos 2011

Clinical Lab Specialist, Illumina

Dir. Bioscience Dev. Workforce Hub,
MiraCosta College

Bridges Program Trainee

↓

Industry Position

↓

COMPASS Leadership Team Membership

Michael Silva, MS

CSU Channel Islands 2012

Sr. Bioprocess Tech, Genentech

Professor,
Solano Community College

Photo sources: K. Wong, Solano College

Creating a Roadmap for Access and Affordability

- $15.6M resulting from revenue sharing provisions of funding was returned to the state and into a Patient Assistance Fund created by Prop 14
- Medical Affairs department created
- Developing a steering committee
- Developing a patient support program