Right now.

GWG Meeting
September 26, 2019

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

2004

CIRM created by Patient Advocates and California Stakeholders-Proposition 71

$3B

Committed to CIRM Mission

1000

Cutting Edge Research & Transformative Programs funded

56 Clinical Trials

First in human, cell & gene medicine, some ready for final marketing approval

>1200 Patients

Patients enrolled in Alpha Clinics Clinical Trials

SOMETHING BETTER THAN HOPE

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GWG Contribution to CIRM: 2005-2019

117 GWG REVIEWS

200+ AVERAGE APPS SUBMITTED PER YEAR

3000+ APPS REVIEWED

750+ TIER 1 SCORES

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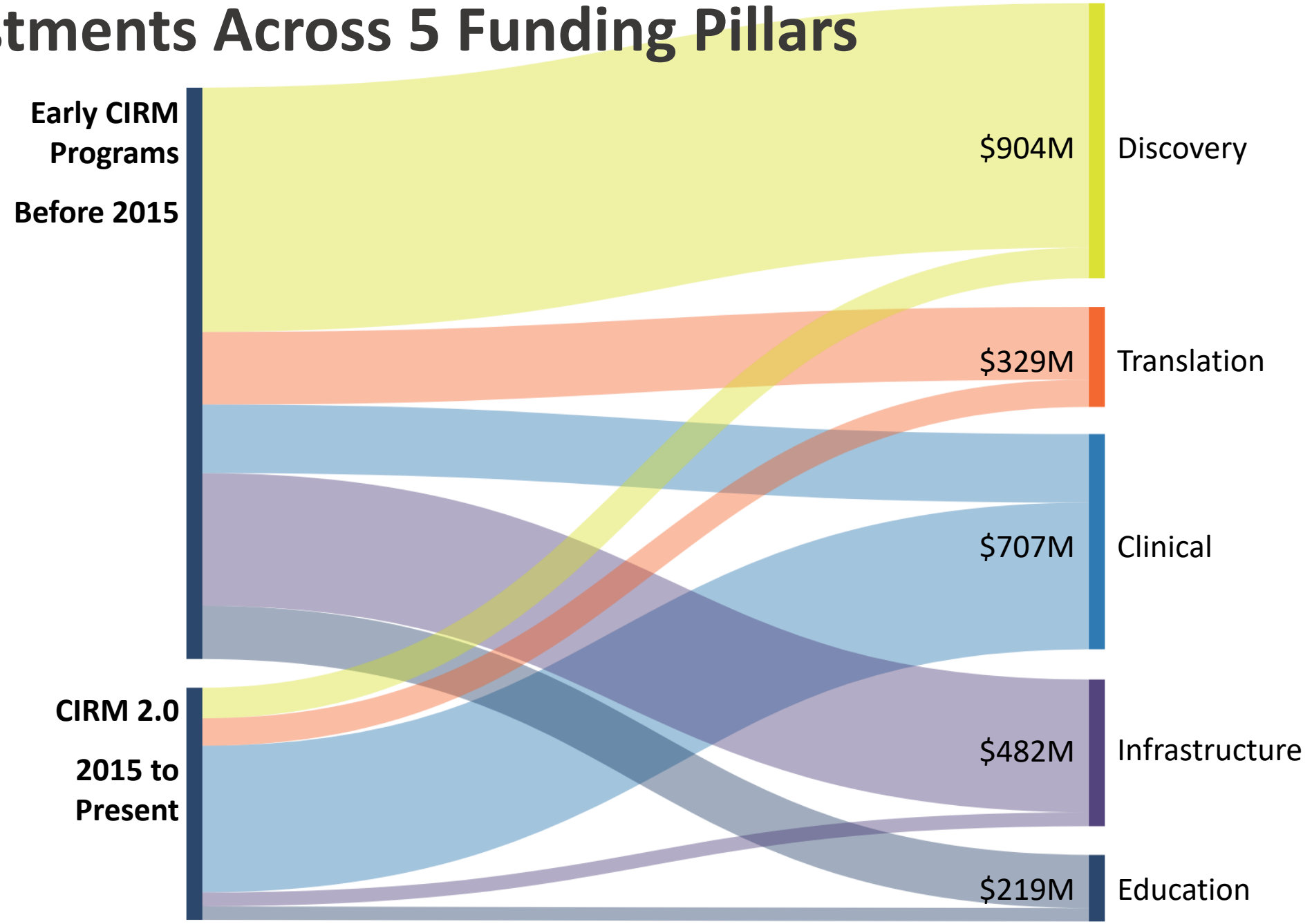
CIRM Investments Across 5 Funding Pillars

$2.6B

1000+

Awards



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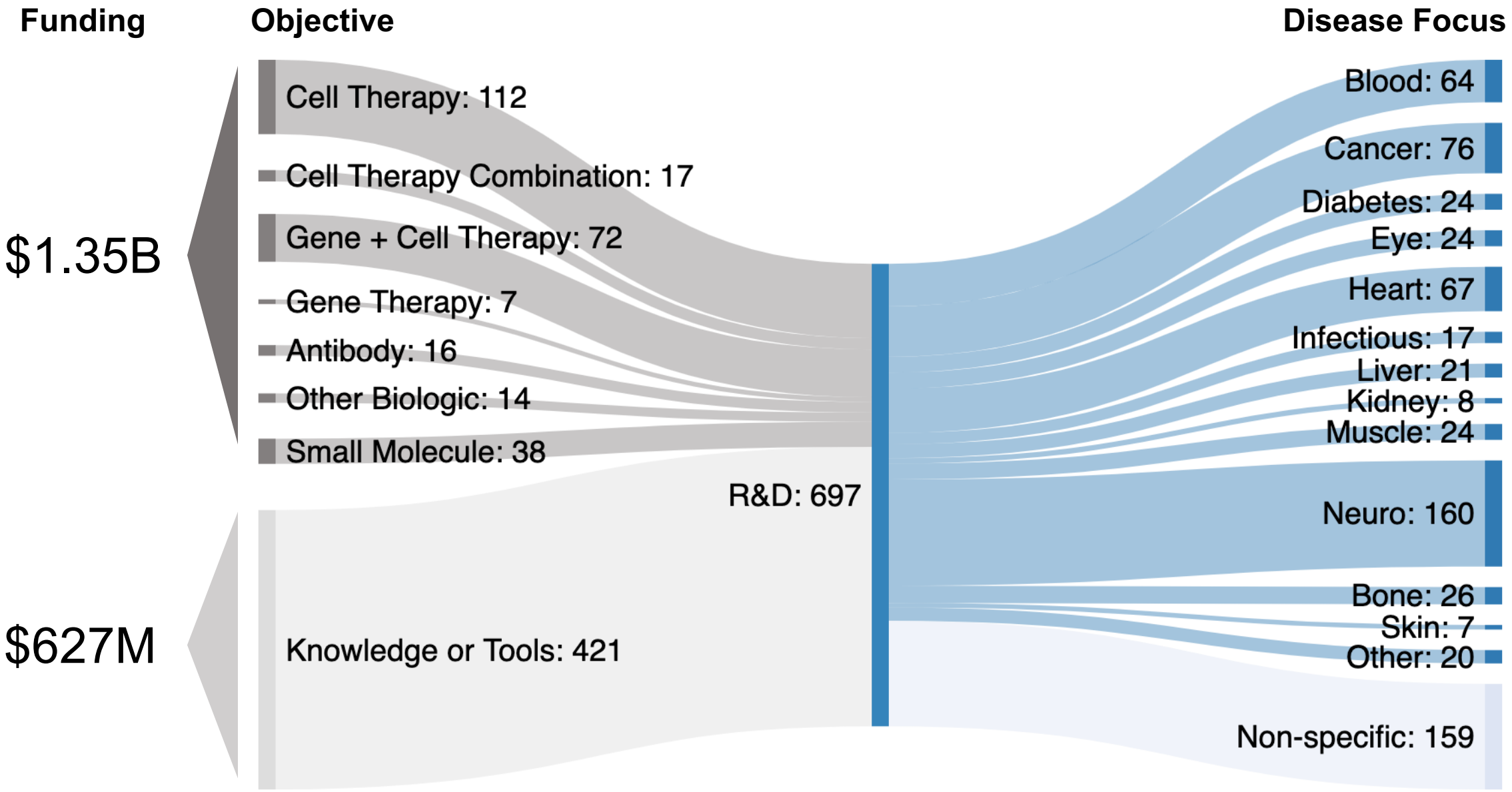
Research & Development Advancing CIRM's Mission: (697 Awards)



Historic Research and Development Grants (Years Active)

SEED, $41M

Comprehensive, $66M

New Faculty, $141M

Tools and Technology, $81M

Early Translational, $237M

Basic Biology, $133M

Disease Team, $406M

Strategic Partnership, $32M

Early awards seeded the field, launched the pipeline

Early awards

2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022

CIRM 2.0

CIRM 2.0 awards focused on therapeutic development

Preclinical Development & Translational, $134M

Inception, $8M

Quest, $93M

Clinical, $492M

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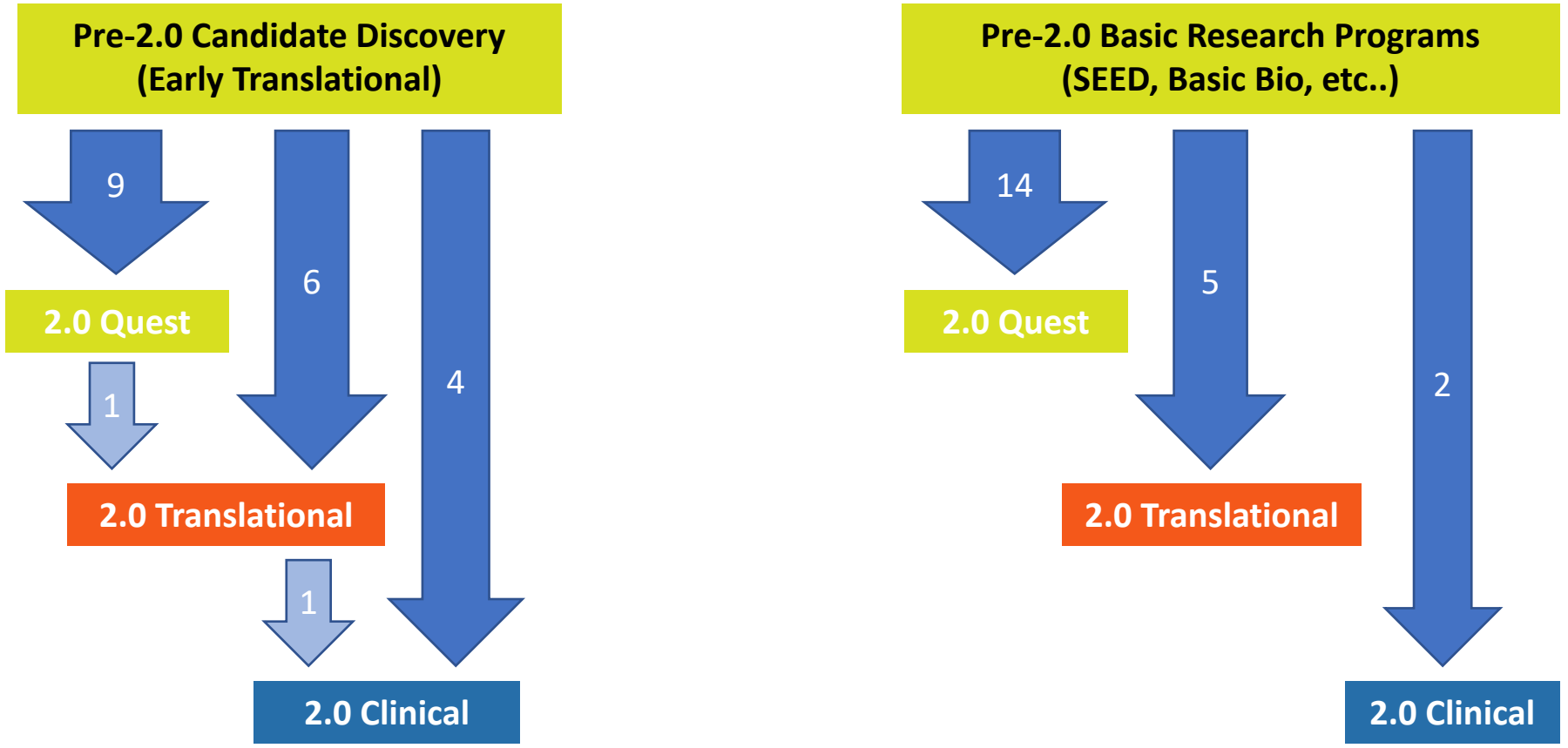
Early Stage Pre-2.0 Projects Feeding CIRM 2.0 Pipeline

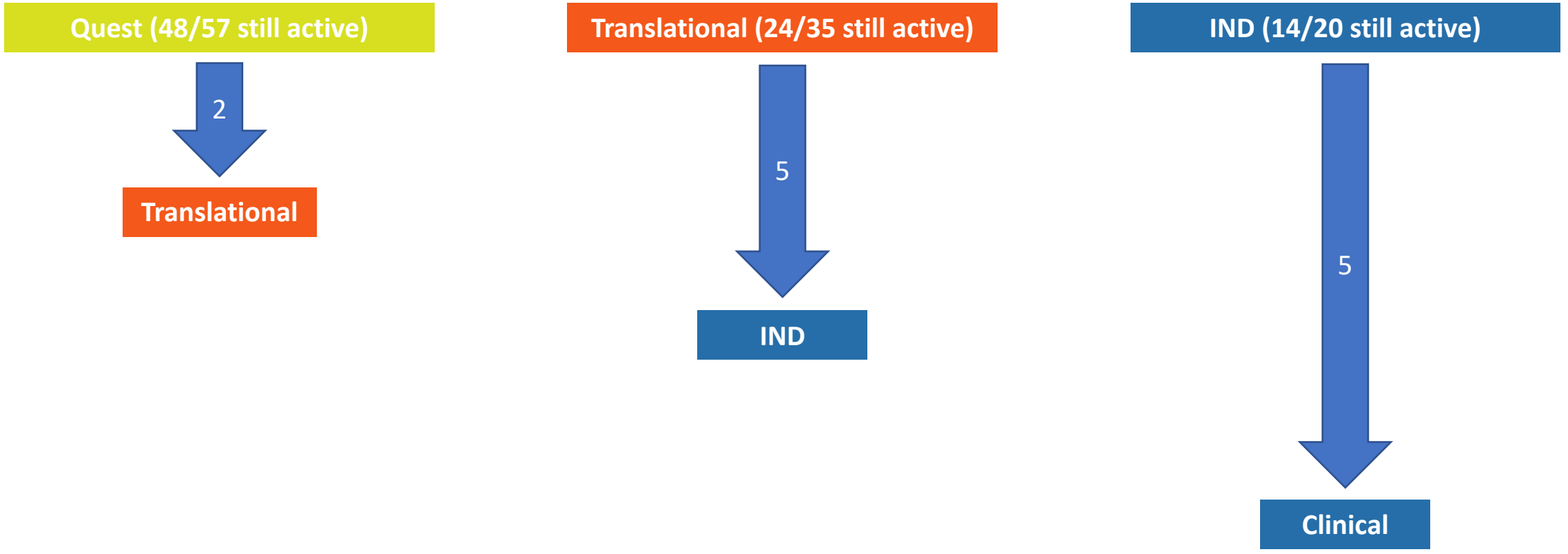
Basic research and candidate discovery pre-CIRM 2.0 projects have entered and advanced within the CIRM 2.0 development pipeline.



Figures exclude progression of projects that entered the pipeline under CIRM 2.0 (see next slide).

CIRM 2.0 Pipeline Progression

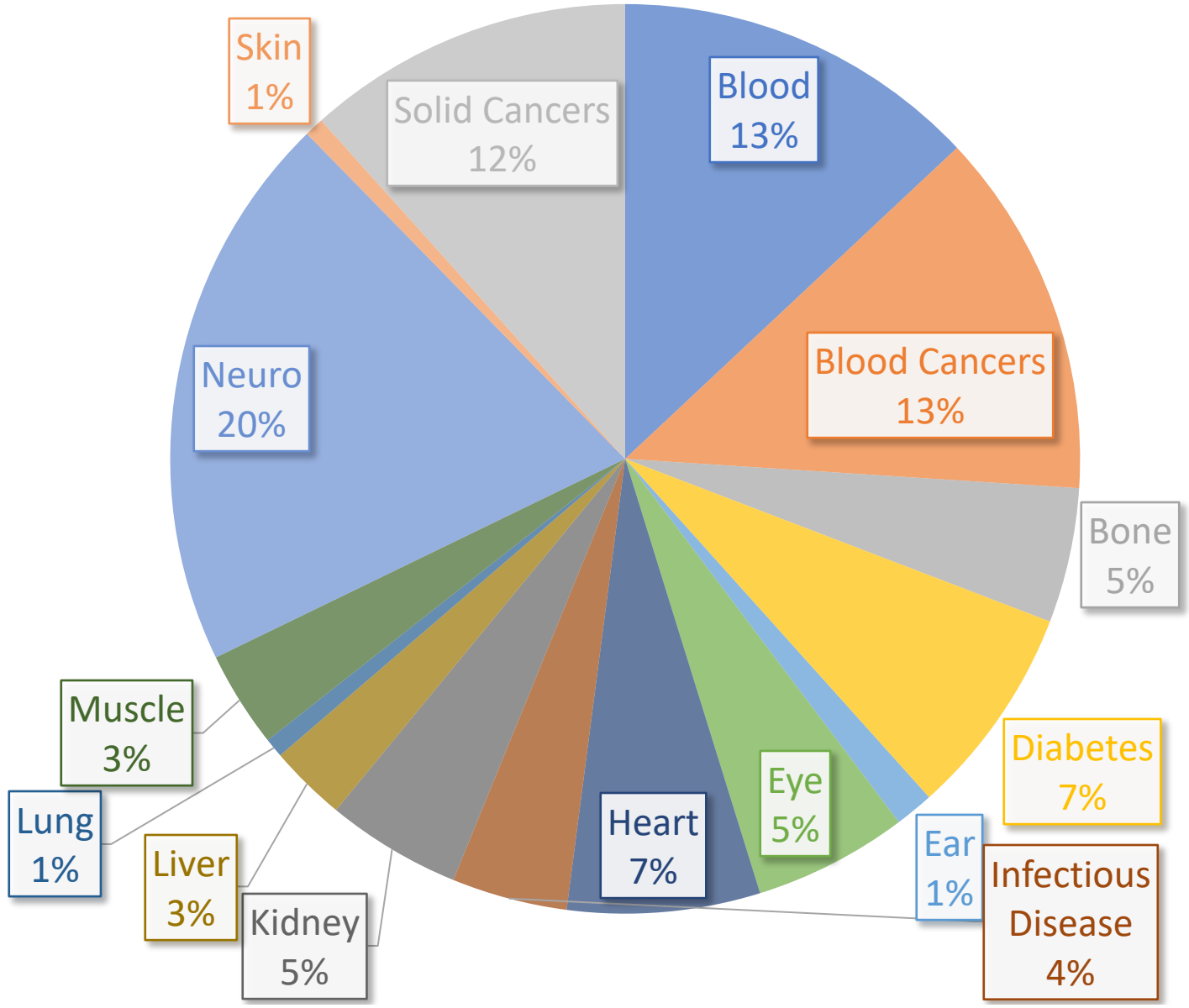
While most awards are still active, some of the completed CIRM 2.0 projects have successfully progressed within the CIRM 2.0 pipeline.



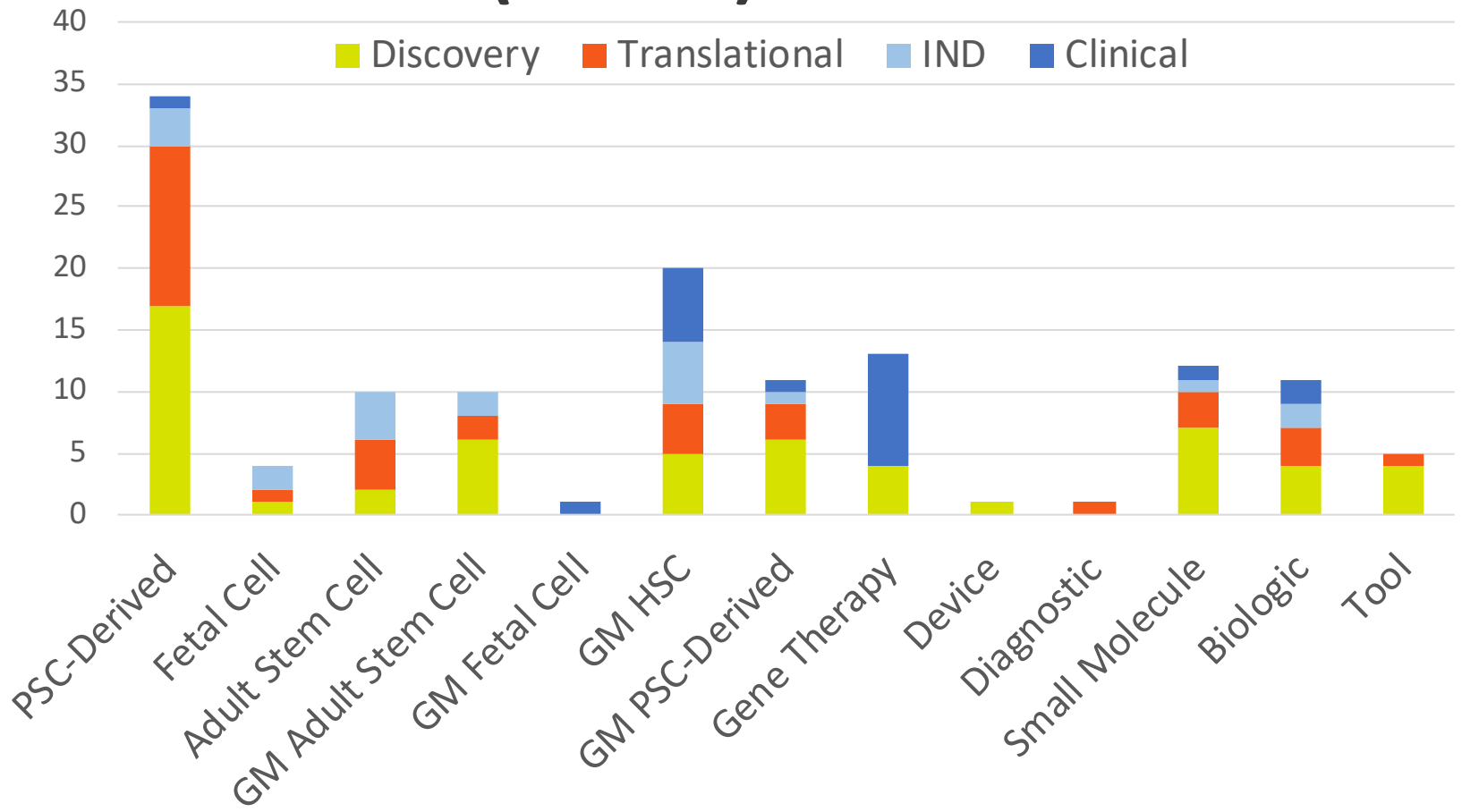
CIRM 2.0 Disease Areas (n=153)

Discrete yet seamless CIRM 2.0 funding opportunities continue to have broad disease representation.

Strong presence in neuro, cancer and blood disorders.



CIRM 2.0 Candidates (n=153)



CIRM 2.0 funding programs cover all therapeutic modalities and technologies eligible for CIRM funding.

- Majority of clinical projects are adult stem cell and gene-modified adult stem cell therapies.
- PSC-derived and gene-modified PSC-derived therapies are more prevalent in preclinical programs.

GM: gene-modified

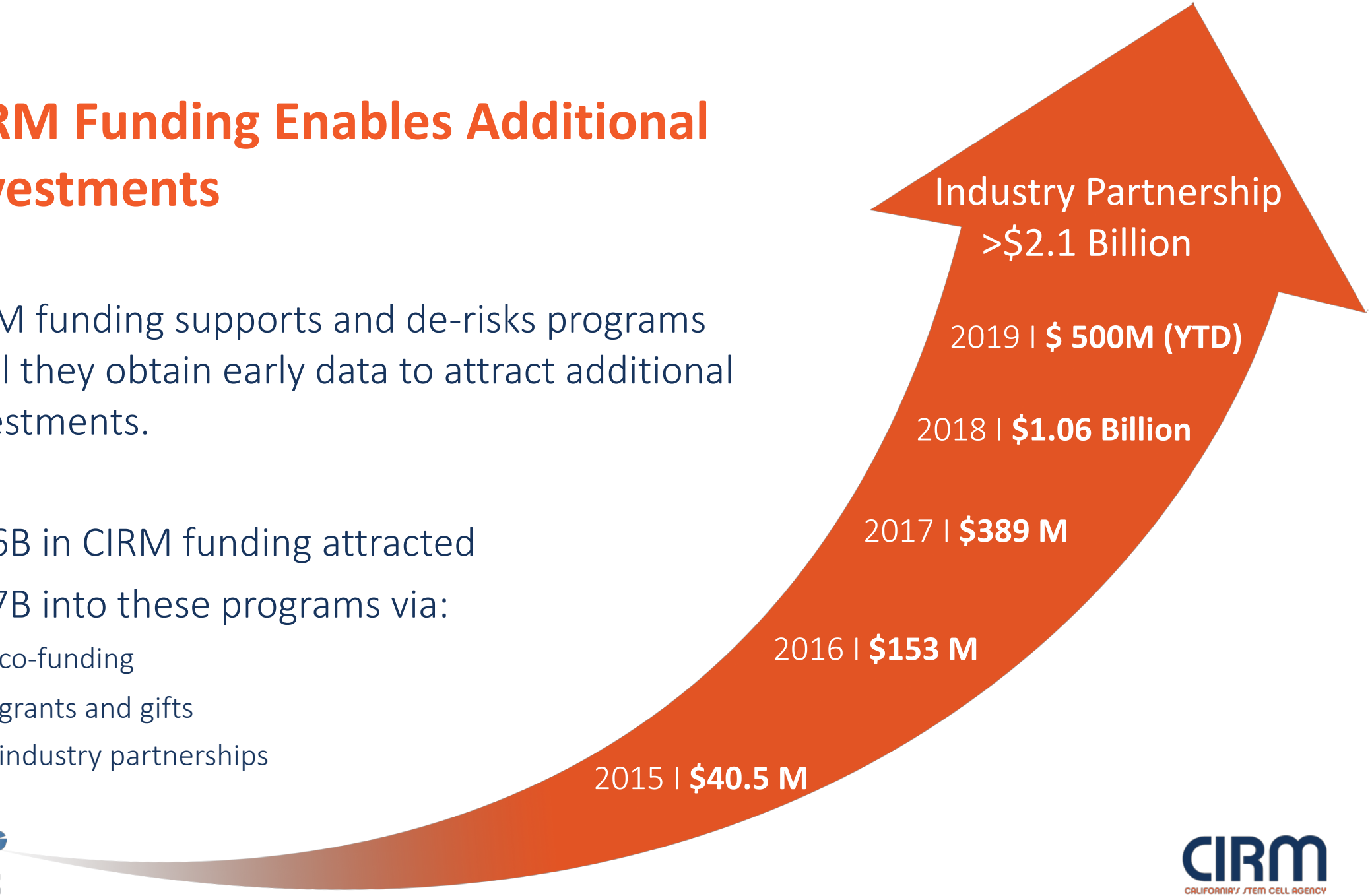
CIRM Funding Enables Additional Investments

CIRM funding supports and de-risks programs until they obtain early data to attract additional investments.

$2.6B in CIRM funding attracted

$3.7B into these programs via:

- co-funding
- grants and gifts
- industry partnerships



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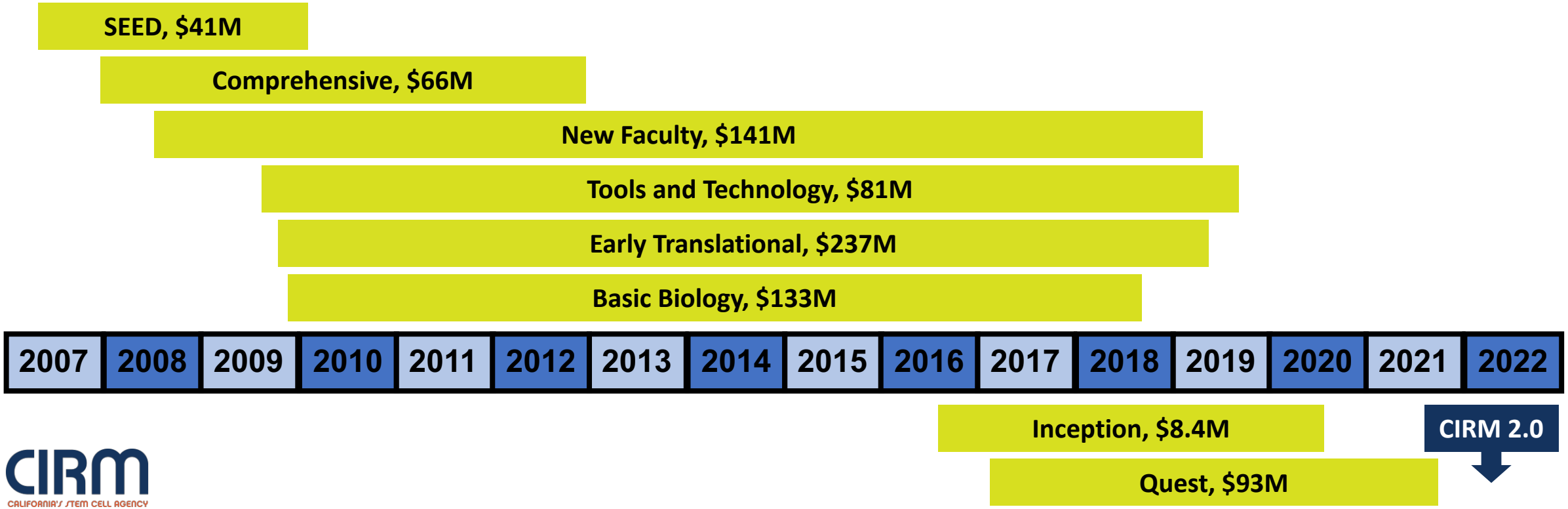
Basic Research & Discovery Overview

DISCOVERY

- **SEED, Comprehensive:** attract new and support established investigators in hESC research
- **Basic Biology:** human stem cell biology, differentiation, mechanisms, disease
- **Early Translational:** therapeutic candidate discovery
- **Tools and Technology:** tools to overcome roadblocks in translation of stem cell research
- **New Faculty:** support promising scientists in the critical early stages of their careers
- **Inception:** seed funding for new ideas in human stem cell research
- **Quest:** therapeutic and tool/technology candidate discovery



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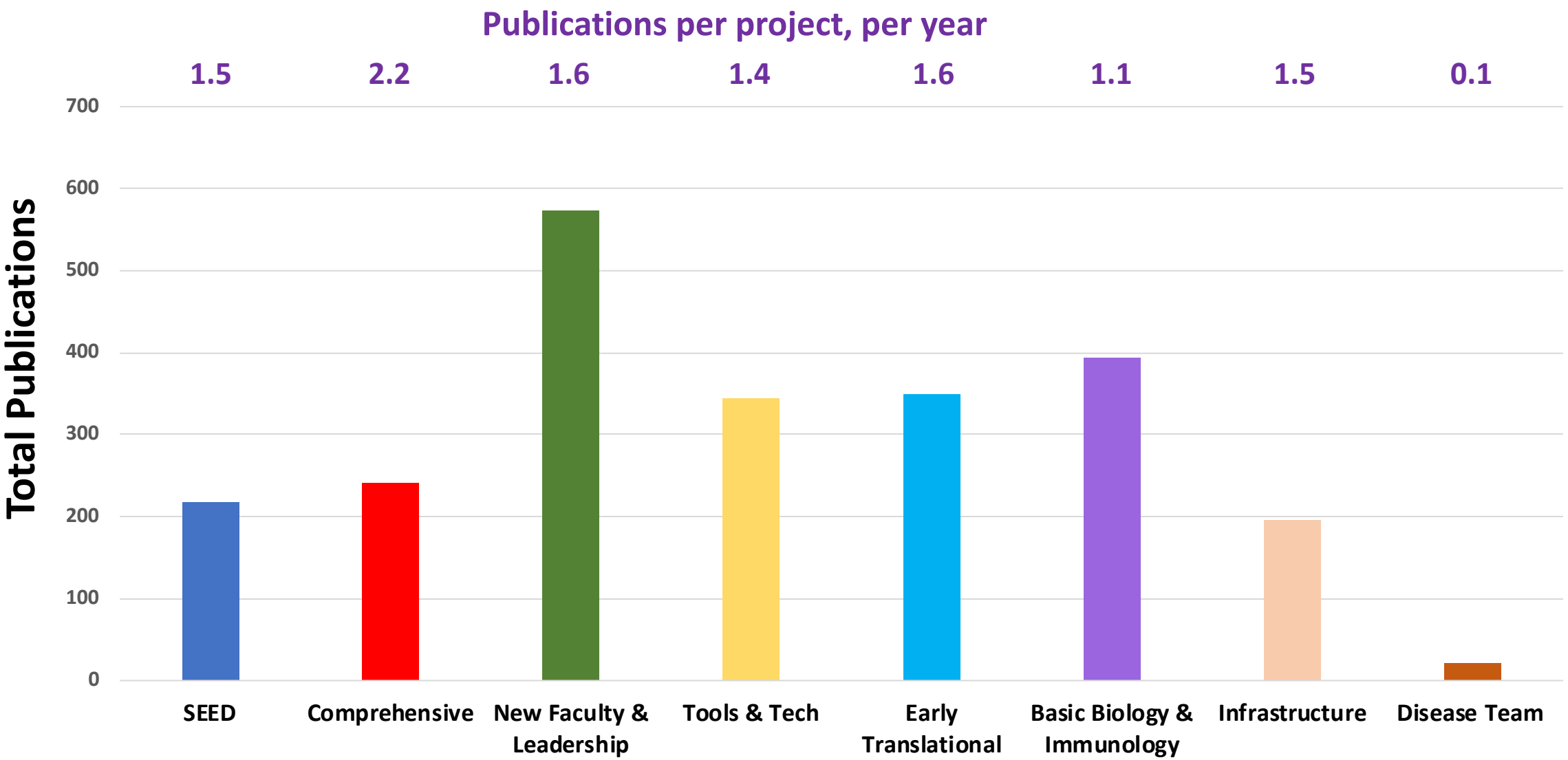
Impact of Early Programs: Publications (2006-present)



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Quest Candidate Discovery Program (2015 to Present)

57 awards

$93M
total funding

18 candidates received prior CIRM funding

DISCOVERY

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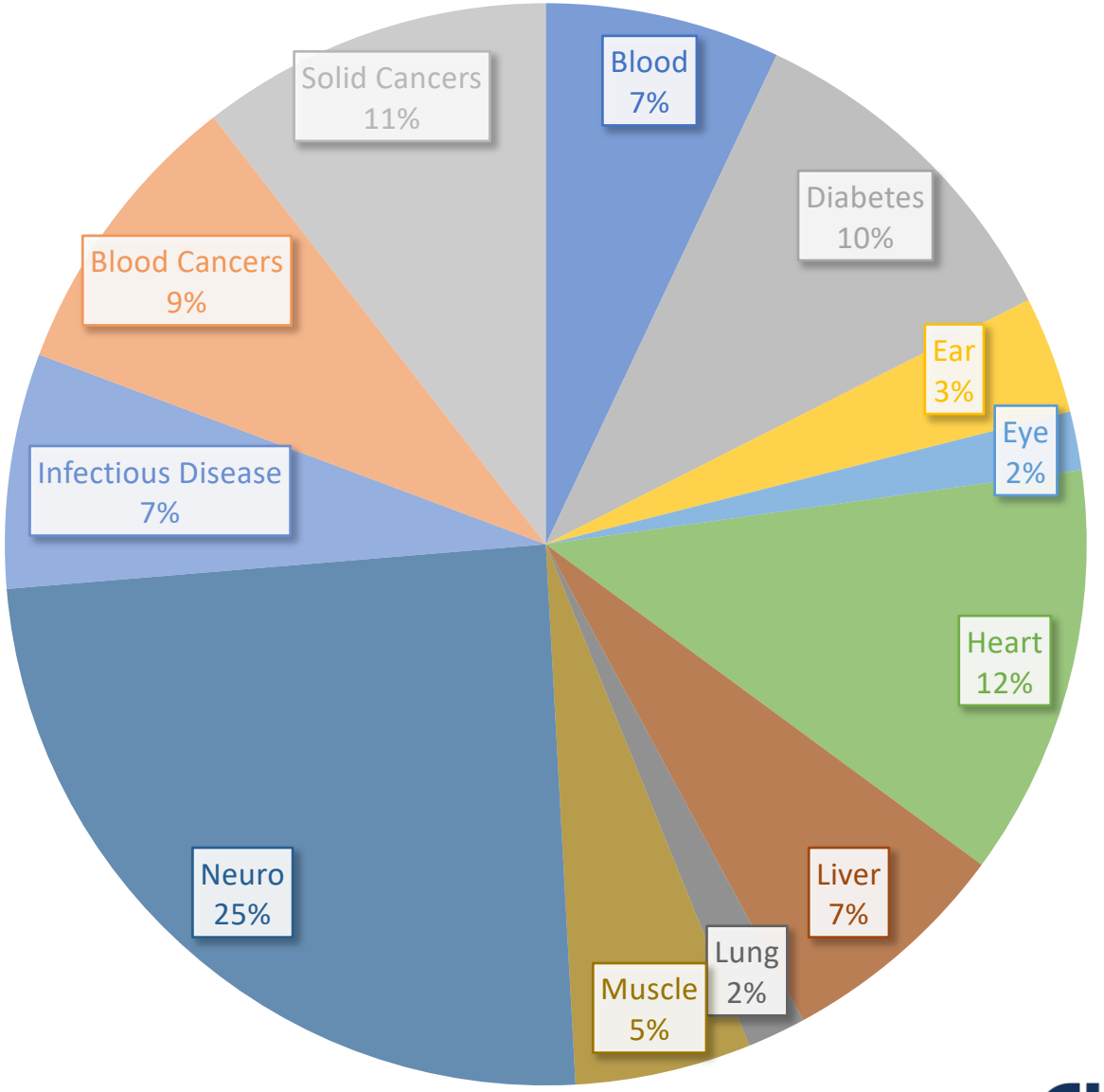
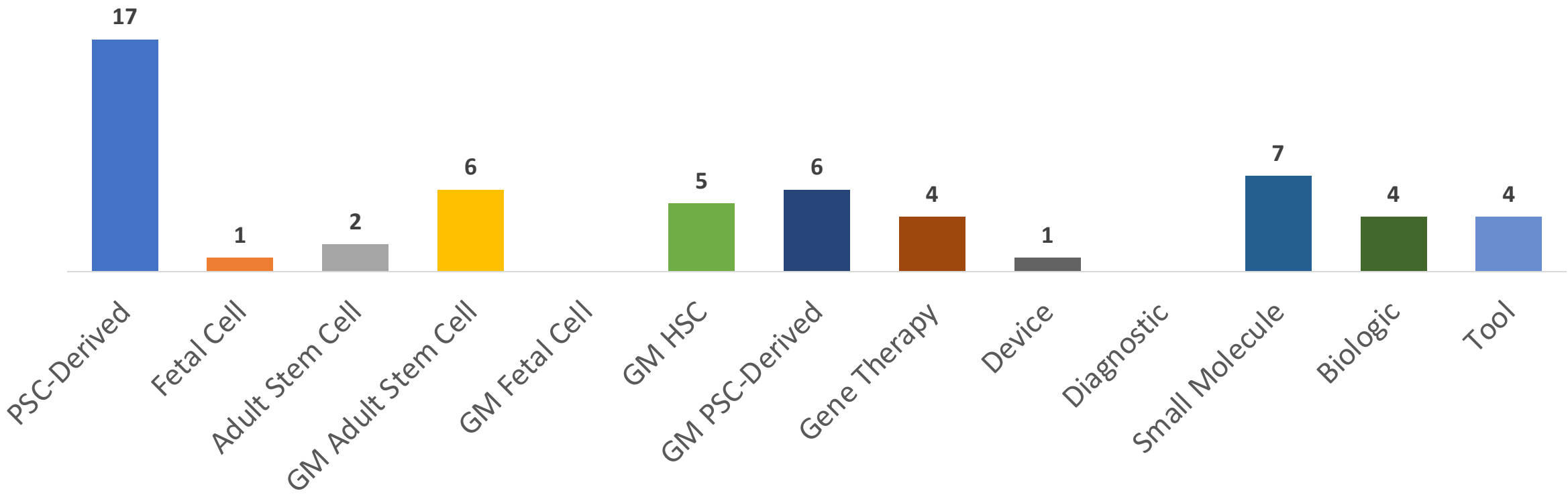
Quest Projects (n=57): Disease Indications

Quest Candidate Discovery Stage Projects have the broadest and most balanced disease area coverage compared to later stage CIRM funding opportunities.

Particularly, neurological disorders and heart disease constitute a higher proportion of this program's portfolio compared to later stage programs.



Quest Projects (n=57): Candidates



PSC-derived cell therapy candidates represent 41% of Quest projects.

Gene-modified cell therapies and gene therapies represent 37% of Quest projects.

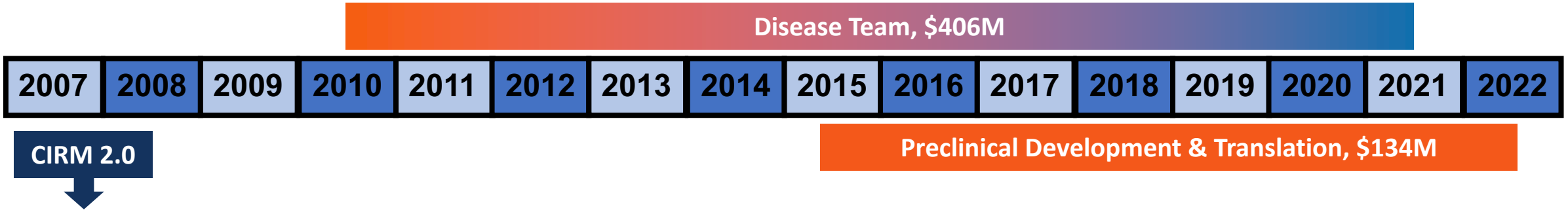
GM: gene-modified

Candidate Discovery Award Outcomes

- 48 out of 57 awards are still active
- 9 awards closed or terminated
- 3 candidates have progressed to translational stage (+1 pending)

Translational Overview

- **Disease Team:** some awards supported translational stage activities as part of a broader objective
- **Preclinical Development:** translational development culminating in pre-IND/IDE meeting
- **Translation:** translational development culminating in pre-IND/IDE meeting



Current Translational Program (2015 to Present)

35 awards

$134M

total funding

12 awards completed

5 progressed to CLIN1

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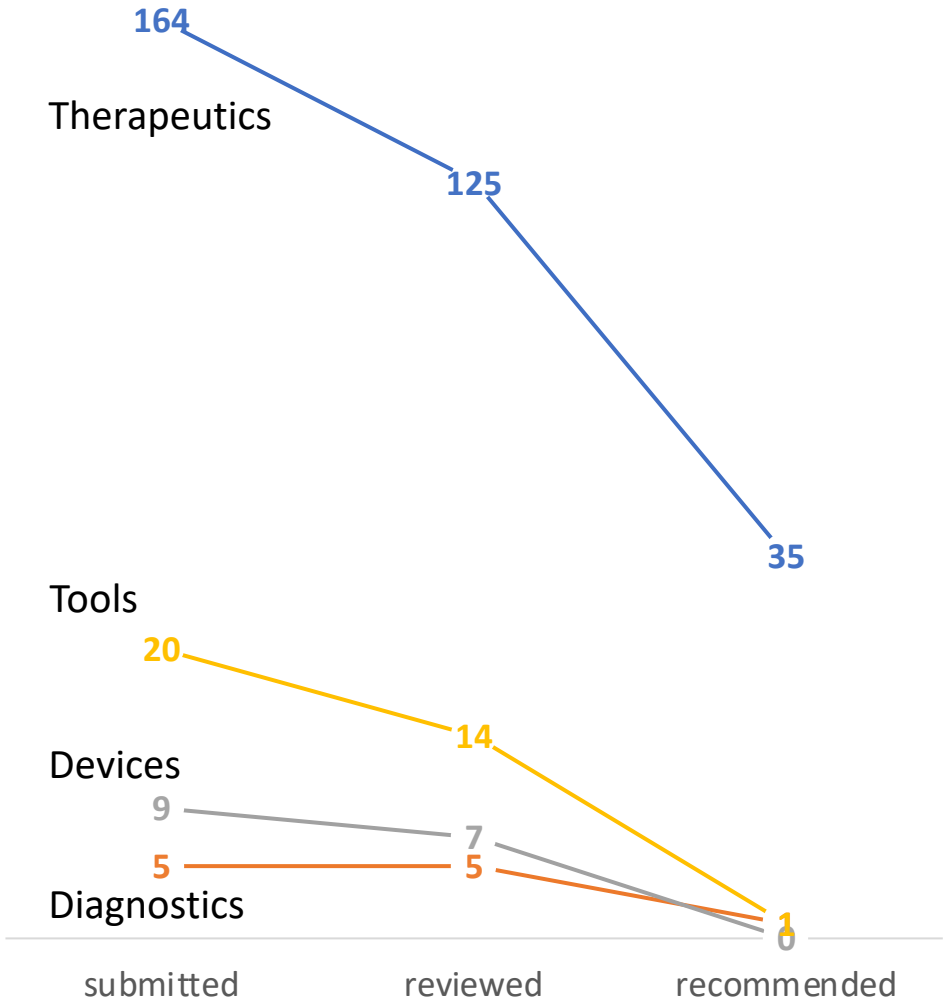
Current Translational Program

- Encompasses funding for translational stage activities for
  - Preclinical Development (PC1)
  - Therapeutics (TRAN1)
  - Diagnostics (TRAN2)
  - Medical devices (TRAN3)
  - Tools (TRAN4)
- Project costs, time limits, activities, and eligibility requirements were dependent on the product type

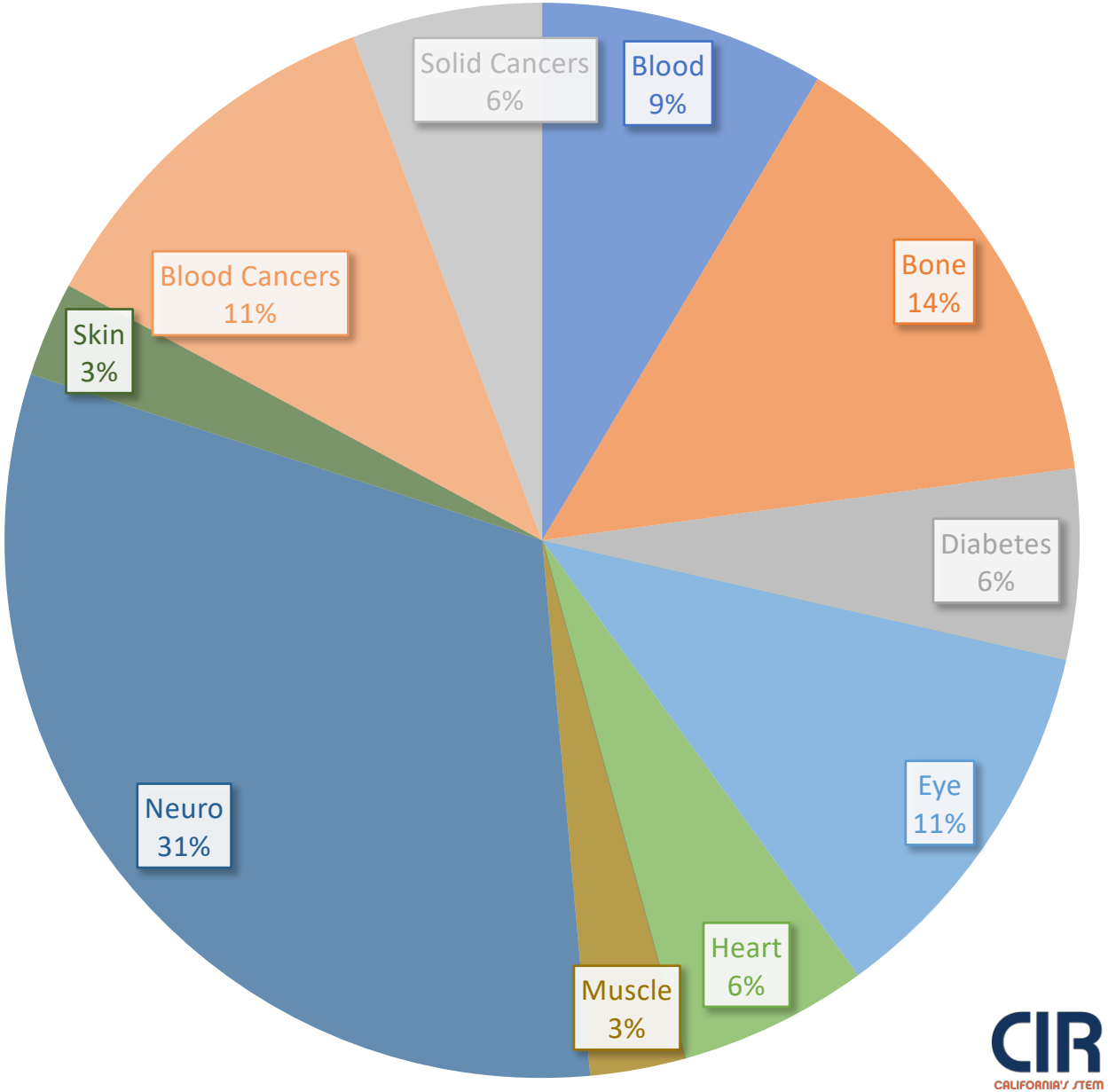
2015-2019 Translational Applications



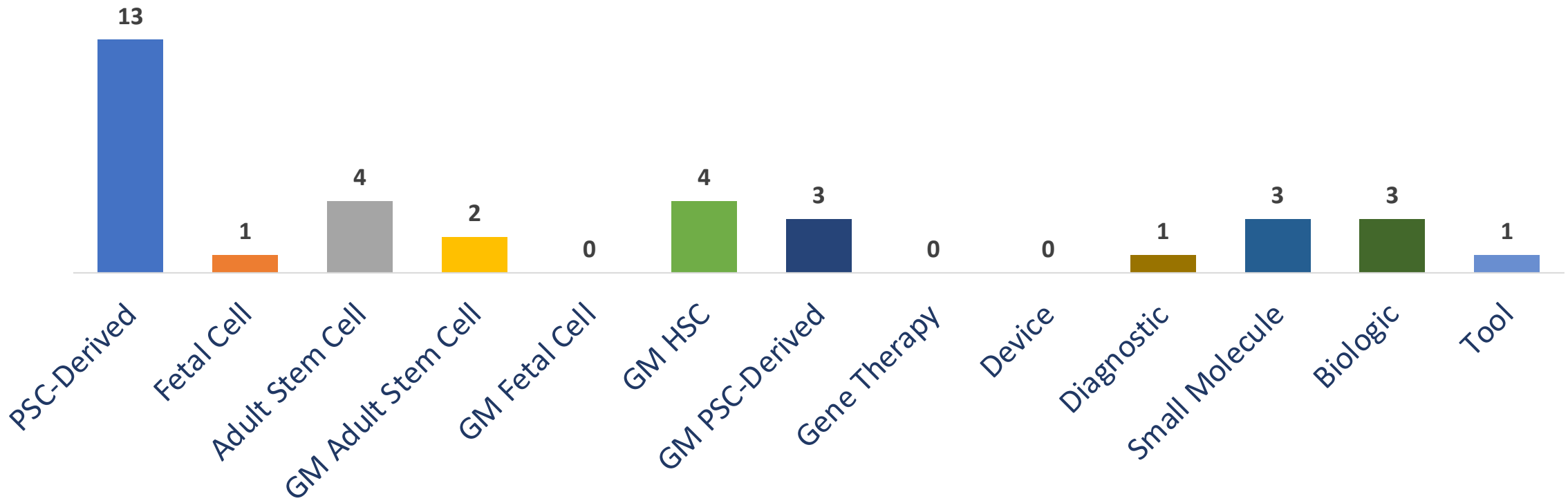
Translational Projects (n=35): Disease Indications

Over 30% of Translational projects are focused on neurological disorders.

- 75% of the neuro projects are developing PSC-derived therapies.



Translational Projects (n=35): Modalities



75% of Translational awards are developing cell therapies.

35% of translational awards are developing PSC-derived cell therapies.

GM: gene-modified

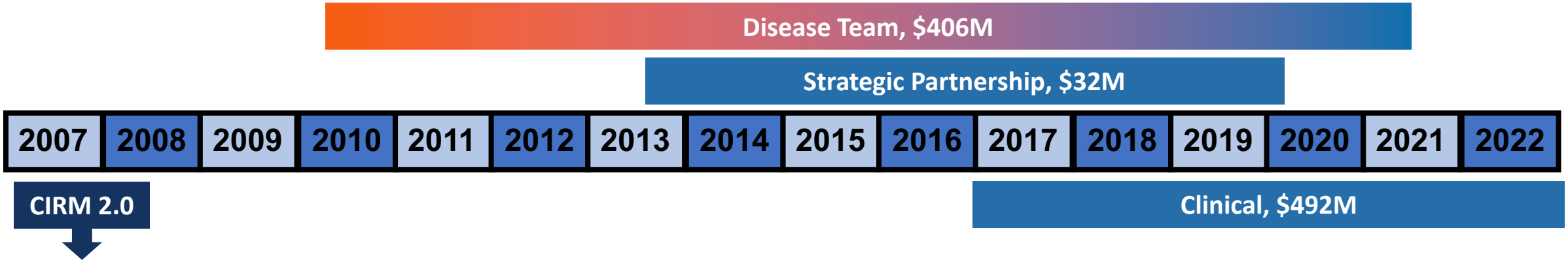
Translational Award Outcomes

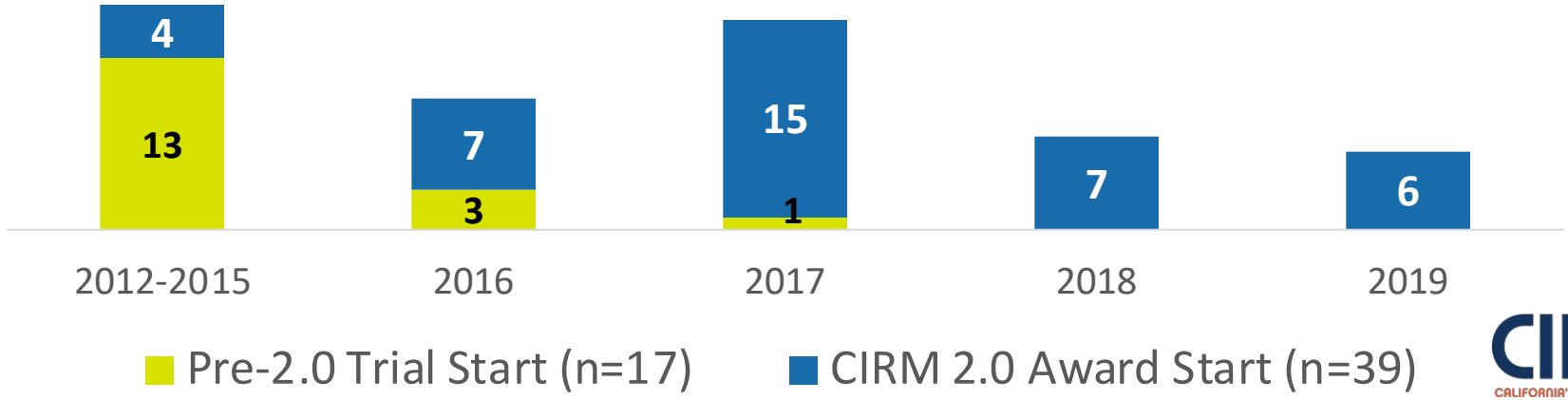
- 24 out of 35 awards are still active
- 8 pre-IND meetings completed or scheduled
- 2 out of 3 terminated awards were due to process development failures
- 5 received follow on CLIN1 Awards to support IND enabling studies
- Pipeline Projects (received prior CIRM funding)
  - 19 projects progressed from early CIRM programs
  - 2 projects progressed from Quest Awards (candidate discovery)

Clinical Overview

- **Disease Team & Strategic Partnership:** A single award spanned multiple development stages from Discovery to Clinical
- **Clinical:** Three types of awards each span a single development stage
  - CLIN1: IND-enabling, CLIN2: Clinical Trials, CLIN3: Registrational Trials

CLINICAL





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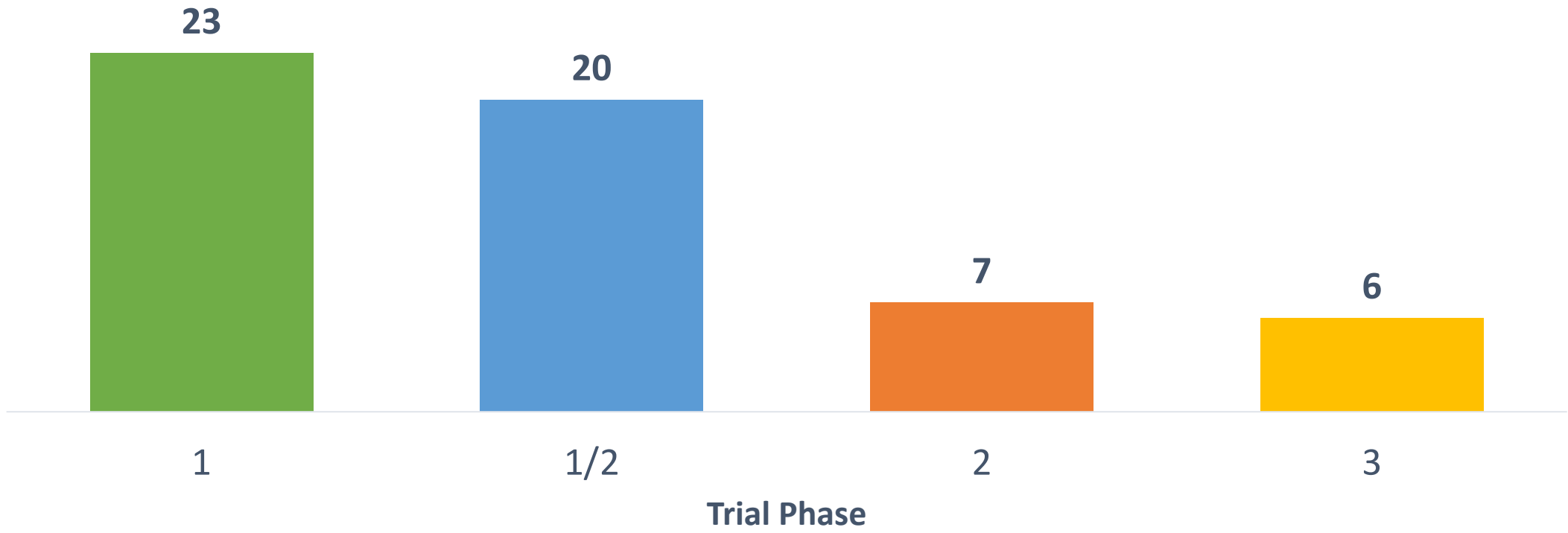
All Clinical Trials (n=56): Phases



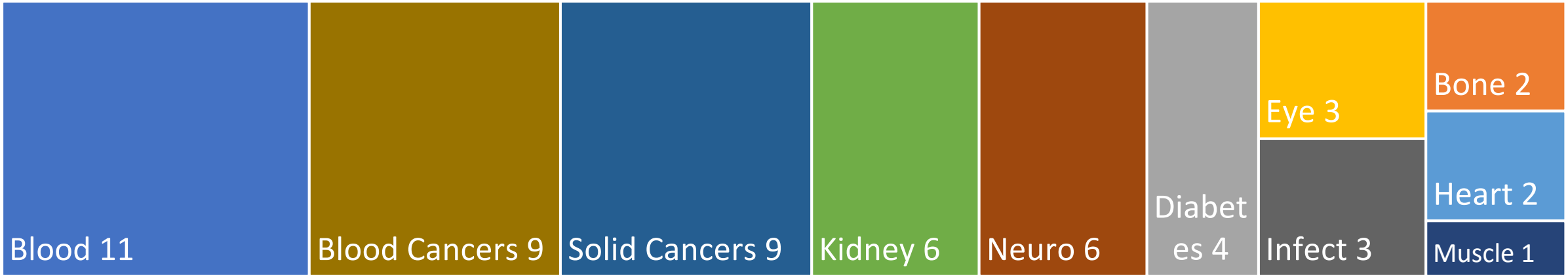
Active Phase 3 Trials

1. Humacyte (AV Dialysis Graft)
2. Medeor (Kidney Transplant Tolerance)
3. Brainstorm (ALS)

Projected BLA Filings
(As publicly reported by Sponsor)

1. Orchard OTL-101: 2020
2. Poseida BCMA-101: Q4 2020

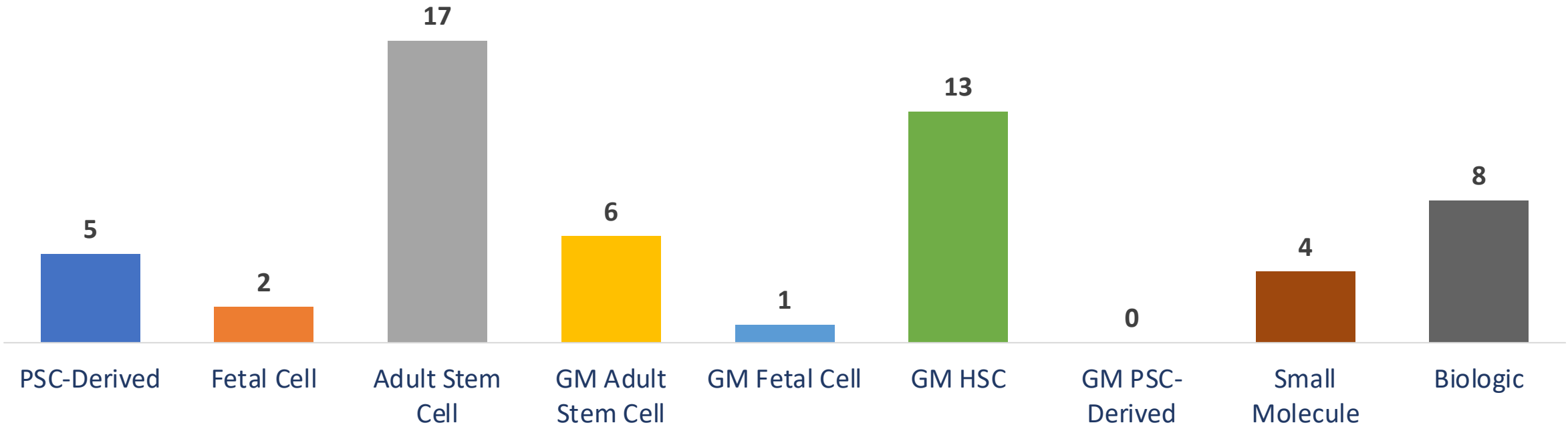
All Clinical Trials (n=56): Disease Areas



CIRM's clinical trials portfolio broadly represents disease areas with significant unmet medical needs.

Blood disorders and cancer are the most prevalent disease areas in CIRM's clinical trials portfolio.

All Clinical Trials (n=56): Therapeutic Modalities



CIRM's clinical trials portfolio is weighted toward adult stem/progenitor cell-based therapies.

Gene-modified cell therapies represent over a third of this portfolio.

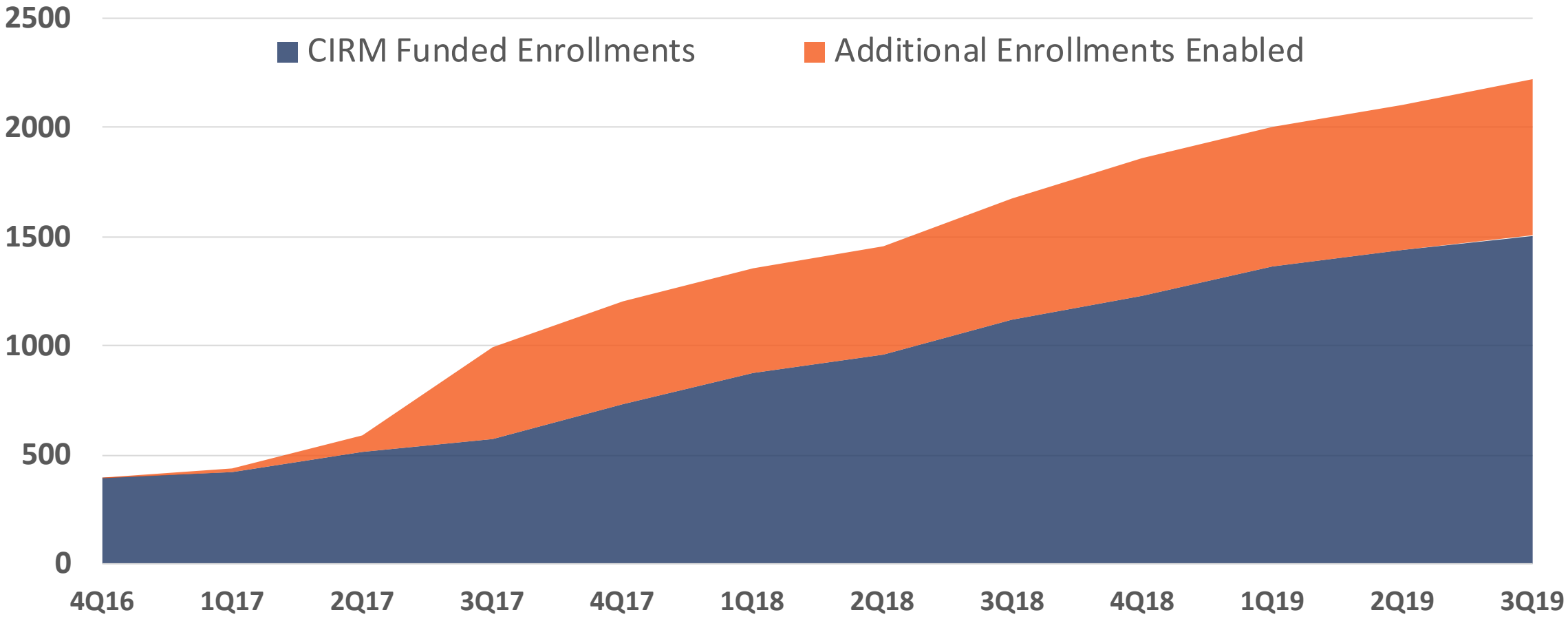
Seven trials are studying gene-modified HSC therapies for blood disorders.

GM: gene-modified

All Clinical Trials: FDA Designations

Grantee	Disease Area	Therapeutic Modality	FDA Designation
Humacyte	Kidney	Biologic	RMAT, Fast Track
jCyte	Eye	Fetal-Derived Cell	RMAT, Orphan Drug
Lineage Cell (Asterias)	Neuro	PSC-Derived Cell	RMAT
Capricor	Neuro	Adult Stem Cell	RMAT
Orchard	Blood	GM HSC	Breakthrough
Brainstorm	Neuro	Adult Stem Cell	Fast Track
Poseida	Cancer	GM Adult Stem Cell	RMAT, Orphan Drug
Medeor	Kidney	Adult Stem Cell	Orphan Drug
St. Jude	Blood	GM HSC	RMAT

All Clinical Trials (n=56): Enrollment



CIRM Funded Enrollments: All enrollments by California awardees and enrollments in California by Non-California awardees.

Additional Enrollments Enabled: All enrollments outside of California by Non-California awardees.

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Current Clinical Program Overview (2015 to Present)

61 awards*

$492M

total funding

5 IND awards progressed to clinical trials

CLINICAL

*CLIN1 and CLIN2

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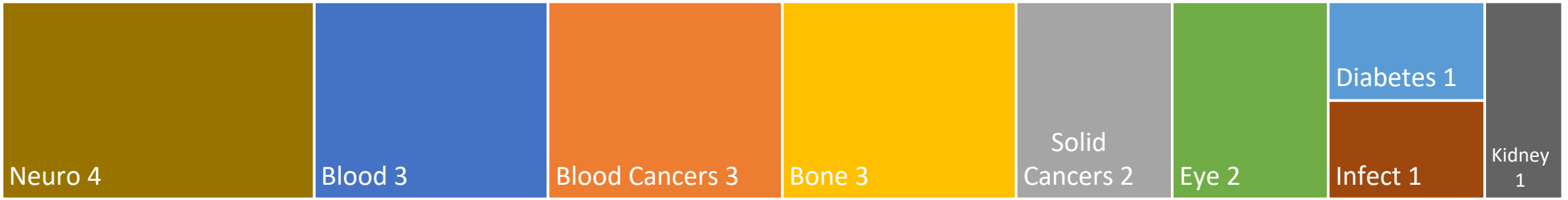
CIRM 2.0 Clinical Awards: Disease Areas

IND Enabling (n=20)



Clinical Trials (n=41)

Broad disease area representation in both clinical funding programs.

Blood Disorders:

- 15% of IND Projects
- 25% of Clinical Trial Projects

Cancer:

- 20% of IND Projects
- 34% of Clinical Trial Projects

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CIRM 2.0 Clinical Awards: Therapeutics Modalities

IND Enabling (n=20)

Clinical Trials (n=41)

Adult Stem Cells:
- 20% of IND Projects
- 36% of Clinical Trial Projects

Gene-modified cell therapies:
- 40% of IND Projects
- 40% of Clinical Trial Projects

Biologics & Small Molecules:
- 40% of IND Projects
- 20% of Clinical Trial Projects

GM: gene-modified

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CIRM 2.0 Clinical Award Outcomes

- IND Enabling Awards (n=20)
  - 7 successfully filed IND
  - 5 progressed to CLIN2
- Clinical Trial Awards (n=41)
  - 2 Trials Completed
  - 2 Trials Terminated

- Pipeline Projects (received prior CIRM funding)
  - 6 IND awards
  - 20 Clinical Trial awards

Infrastructure Overview

7 initiatives

$482M

total funding

48 awards

INFRASTRUCTURE

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Infrastructure Overview

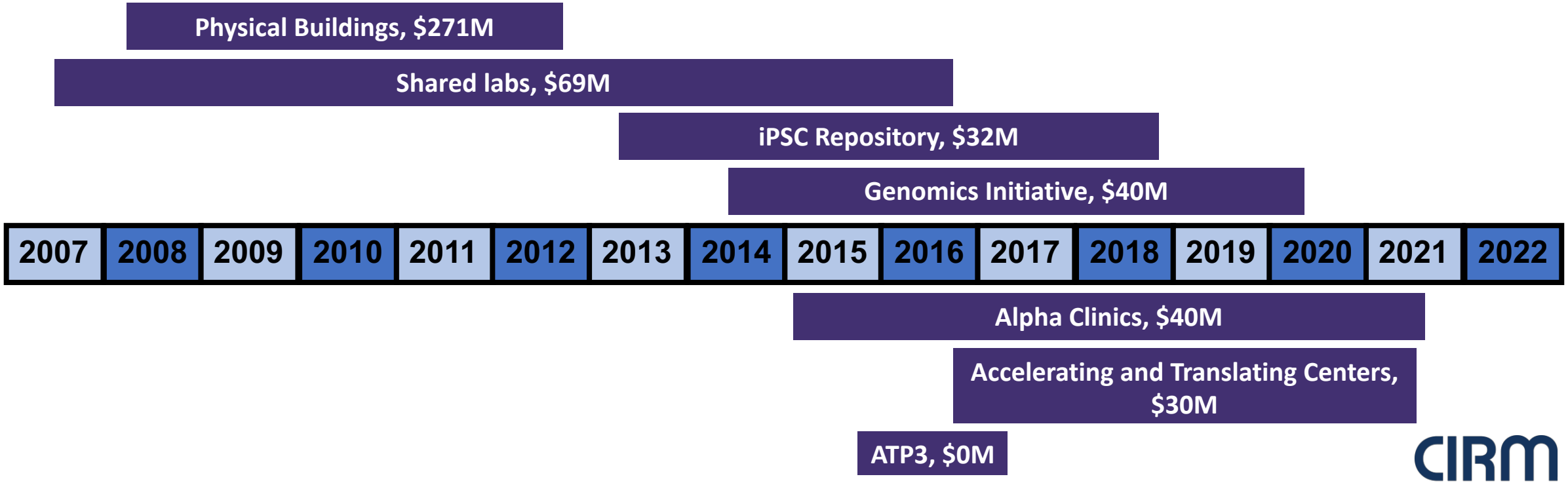
Buildings and Labs
- Physical Buildings
- Shared Labs

Therapy Development
- Alpha Clinics
- Accelerating Center
- Translating Center

Research
- iPSC Repository
- Genomics Initiative

Business
- ATP3

INFRASTRUCTURE



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Physical Infrastructure

12 institutions funded throughout California

Historical rationale to enable hESC research

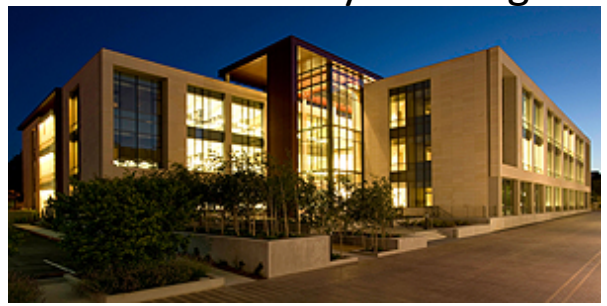
- 12 research facilities – institutional use
- 1 GMP facility (UCD) – several outside institutional clients

Total direct CIRM funding: $271M

Private/Institutional funding: $543M

Buck Institute	UC Berkeley
Sanford Burnham Institute	UC Davis
Stanford	UC Irvine
USC	UC Los Angeles
	UC Merced
	UC San Francisco
	UC Santa Cruz
	UC Santa Barbara

Stanford Lokey Building



UC Davis GMP facility

Shared Labs

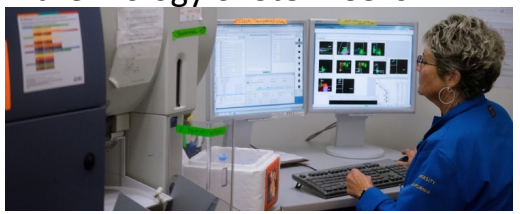
Creation of dedicated laboratory spaces for the culture and maintenance of hESCs

Historical rationale to enable hESC research independent of federal restrictions

Total CIRM funding: $69M

- 17 core facilities
  - Buck Institute
  - Children's Hospital LA
  - Gladstone Institute
  - Salk Institute
  - Sanford-Burnham Institute
  - Scripps Research Institute
  - Stanford University
  - USC
  - UC Berkeley
  - UC Davis
  - UC Irvine
  - UC Los Angeles
  - UC Riverside
  - UC San Diego
  - UC San Francisco
  - UC Santa Cruz
  - UC Santa Barbara
- 90+ hESC cell lines derived
- 173 publications
- hESC training courses established

UC Santa Cruz Institute for the Biology of Stem Cells



Research Infrastructure – iPSC Repository

9 awards totaling $32M

- Centralized iPSC bank
  - Lines owned by CIRM
  - Lines banked and distributed by FujiFilm Cellular Dynamics
- 2400 unique lines created with uniform production method
- Standardized consent language
- IP agreement to use lines commercially
- Clinical and demographic information, but no access to longitudinal studies from donors
- ~1000 lines sold

fujifilmcdi.com/the-cirm-ipsc-bank/

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Research Infrastructure – Genomics Initiative

3 awards totaling $40M

- Consortium for academic projects with major genomics components – over 20 laboratories
- 2 central sequencing centers (Stanford and Salk)
- 1 data hub (UCSC)
- Diverse projects with uniform data processing and organization for analysis
- Shift to single cell sequencing
- Most funds used for data collection

The Stem Cell Hub
Center for Excellence in Stem Cell Genomics

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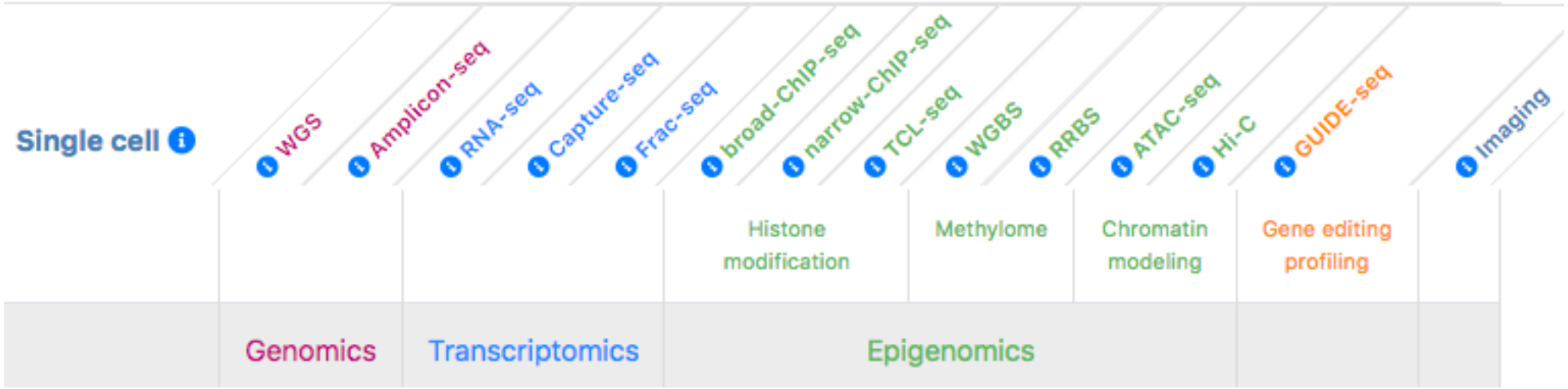
cirm.ucsc.edu



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Development Infrastructure – Alpha Clinics

$40M to fund 5 sites

- City of Hope
- UCLA/UCI
- UCSD
- UCSF
- UC Davis

CIRM ALPHA CLINICS
Delivering Patient Treatments

Medical clinics specializing in delivering cell therapies to patients

- Trial sites for 97 sponsored programs (CIRM and non-CIRM)
- 493 patients enrolled
- Shared protocols
- IRB Reliance agreement
- MD fellowships (UCD, UCSF)

Trials supported by Alpha Clinics (n=97)

CIRM ALPHA CLINICS
Delivering Patient Treatments

Number of Trials by Technology Type		%
Engineered Immune Cells	40	44.9%
Hematopoietic (HSC) Derivative	20	22.5%
Embryonic (hESC) Derivative	6	6.7%
Mesenchymal (MSC) Derivative	6	6.7%
Small Molecule or Biologic	3	3.4%
Non-Cellular Gene Therapy	2	2.2%
Other (e.g. observational studies)	20	22.5%

- 65% industry sponsored
- 35% academic sponsored

Number of Trials by Cell Type	
1. Autologous	58
2. Allogeneic	28
3. Not Applicable	11

https://www.cirm.ca.gov/patients/alpha-clinics-network/alpha-clinics-trials

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Development Infrastructure

Cell And Gene Therapy Center | IQVIA™

An integrated information and technology-enabled global healthcare service provider for cell and gene therapies

Accelerating Center - $15M award

- Cell therapy focused CRO
- Services offered:
  - clinical operations
  - regulatory support
  - pharmacoeconomics
  - commercial services

Translating Center - $15M award

- IQVIA CGTC with partners City of Hope, Charles River Labs, and WuXi AppTec
- Services offered:
  - project management
  - regulatory strategy
  - GMP manufacturing
  - preclinical animal studies

Business Infrastructure – ATP3

Accelerating Therapies Public Private Partnership

- Award would allocate $75M with an equal match from the applicant to create a stem cell focused enterprise to commercialize CIRM funded products

- A single applicant organization provides a business plan to in-license and advance to commercial development CIRM-funded technologies from the current IP holders at universities, non-profit research institutions, and for-profit companies. The Company would be expected to be sustainable and exhibit growth beyond the five-year award period.

- RFA did not proceed to review

Education & Training Overview

54 Programs

$219M

total funding

2700+ alumni

EDUCATION

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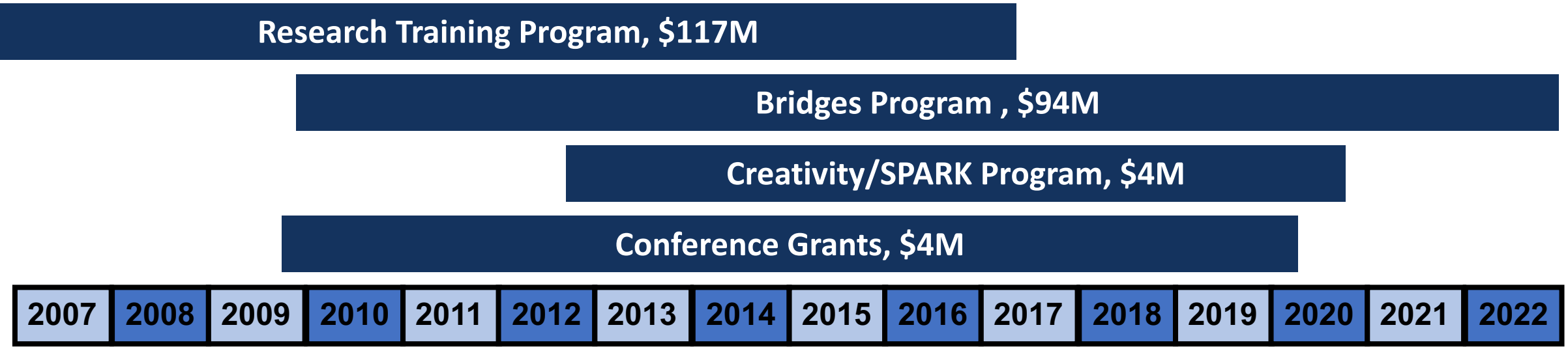
Education and Training Programs Overview

- **Creativity/SPARK:** high school summer internships in stem cell laboratories
- **Bridges Program:** undergraduate, Masters level training and certificates of expertise
- **Research Training Program:** predoctoral, postdoctoral and clinical fellowships
- **Conference Grants:** sponsorship of scientific conferences with relevance to CIRM's mission

EDUCATION



Training Programs Impact 2005-2019

HIGH SCHOOL

9 programs
454* trained

UNDERGRAD/MASTERS

16 programs
1427* trained

PRE/POSTDOCTORAL, CLINICAL

18 programs
940 trained

*Alumni and Presently Completing

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

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Creativity/SPARK Program Overview (2012-2020)

- Creativity/SPARK grants fund summer stem cell internships for high school students at world class university and research institutions in California
- Interns learn about stem cells and regenerative medicine, conduct research, and present their work at the annual SPARK conference
- 9 programs implemented (7 active) across California
- 484 students trained* to date

*Alumni and Presently Completing

Bridges Program Overview (2009-2020)

- Bridges targets undergraduate and Masters students at California universities and colleges that do not have major stem cell research programs of their own
- After completing coursework, students conduct research at “host” laboratories at major research universities, medical schools and/or biotechnology companies
- Students receive training in cell therapy development and participate in patient engagement and outreach activities that engage California’s diverse communities
- 16 programs implemented (14 active) across California
- 1419 students trained to date (alumni and completing); 50% 50% are employed in research labs; 30% are pursuing PhDs, MDs or other professional degrees

Research Training Program and Outcomes (2006-2015)

- Research Training Grants supported the training and development of "CIRM Scholars" at the predoctoral, postdoctoral, and clinical fellow levels, as future leaders of effective stem cell research programs
- 18 programs implemented across California
- Programs were tailored to align scope (level of training) and capitalize on scientific strengths of each institution
- 940 alumni; 1100 scientific publications reported to CIRM
- Research Training Grants were not formally renewed in 2016, as CIRM's direct funding of predoctoral, postdoctoral and clinical fellows through CIRM-sponsored research grants served the same needs and allowed better alignment with CIRM's mission as it evolved