

SOMETHING BETTER THAN HOPE

President's Report



12/21/20

Maria T. Millan, M.D.
President & CEO
California Institute for Regenerative Medicine
December 21, 2020 ICOC Meeting

President's Report:

- The Final Outcome of CIRM's 2016-2020 Strategic Plan
- Update on the CIRM Beyond 2020 Strategic Planning Process
- Update from CIRM Programs
 - Abba Creasey, PhD- Clinical Programs and CIRM Conferences
 - Kent Fitzgerald, PhD- Discovery, Translational and Education Programs
 - Shyam Patel, PhD- Business Development and Industry Alliance Program



2004

CIRM created by Patient Advocates and California Stakeholders-Proposition 71

\$3B

Committed to CIRM Mission

1027 Awards (200 under active management)

Cutting Edge Research & Transformative Programs funded

68 Clinical Trials

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

>2700 Patients

Patients enrolled in CIRM Funded Clinical Trials

2020

\$5.5B Bond Initiative – Proposition 14

CIRM 5-yr Strategic Goals 2016-2020



DISCOVER
46 of target 50
NEW CANDIDATES*

**limited by remaining
Prop 71 funds*



ADVANCE
74 projects progressed
100% increase



REFINE REGULATORY
8 expedited FDA RMATs
(21st Century Cures Act)



**SHORTEN TIME TO
CLINICAL TESTING**

73% CLIN1
achieved IND in 2
years

Time from TRAN to
CLIN1 4.18 years



EXPAND
51 of target 50
NEW TRIALS
68 Total
(>2700 Enrolled)



**INCREASE INDUSTRY
PULL**
63% partnered
72 events
\$12.9B Industry Investment

2020 Update:

1 NEW CANDIDATE

2 Progression Events

2 RMATs

4 CLIN1s filed INDs
2 TRAN1 filed pre-IND

8 trials

4 projects partnered
\$9.6B

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Strategic Plan Process:

Feb 2020 ICOC: Introduction of Strategic Themes

- Advance World Class Science
- Build Pathways to Commercialization
- Increase Patient Access to Innovative Treatments
- Maximize Impact through Operational Excellence

June 2020 ICOC: Board Discussion and Input re. Strategic Themes & Concepts

H2 2020: “Deep Dive” into Strategic Concepts with Board, patient advocates, external advisors and key opinion leaders

Q4 2020: Update on Strategic Concepts for further development

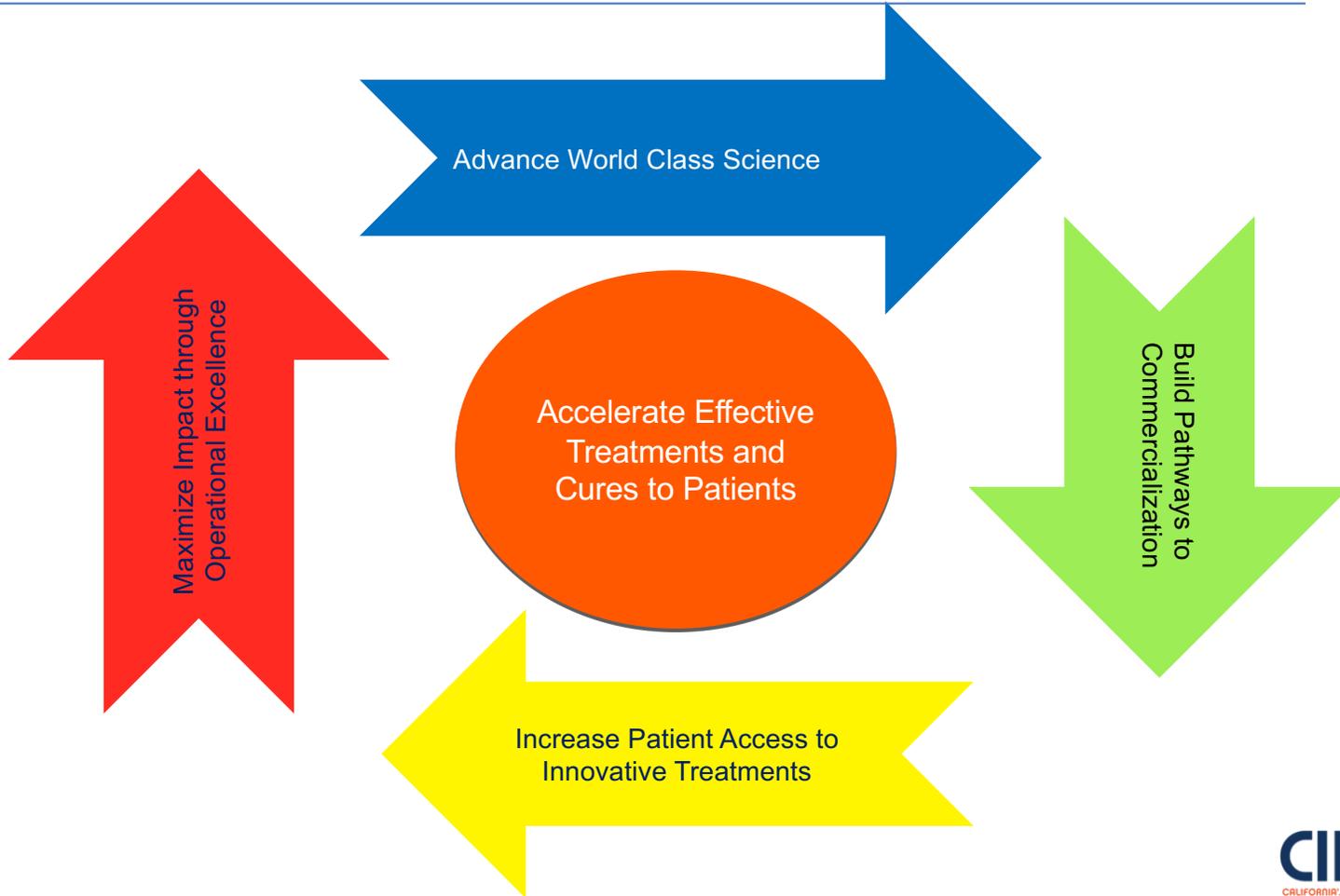
Q1 2021 ICOC: Draft Strategic Plan

H1 2021 ICOC: Adoption of Strategic Plan for CIRM Beyond 2020

Progress on Strategic Plan for CIRM Beyond 2020



Strategic Themes:



Review of Strategic Principles from June 2020 ICOC

- Build on Established CIRM Funding Mechanism
 - *Utilize & build upon existing pillars DISC, TRAN, CLIN, EDU, INFR*
- Data Sharing and Data Access built into funding model
- Lateral integration of pillars and vertical integration of funding opportunities to enable consortium model "Moon Shot"
- A proactive "Quality by design" approach for scientific programs (from DISC2-TRAN-CLIN)
 - "development ready" for regulatory pathway to clinics
 - "tech transfer ready" for manufacture scale up & commercialization
- Tackle Challenges to commercialization and equitable access to treatments and trials

Update on Concepts for Advancing World Class Science

Accelerating Scientific Advancements	<p>Topics discussed at Grantee Meeting Panel with external KOL's and ICOC workgroups:</p> <ul style="list-style-type: none"> • Built-in collaborations • Shared technology networks • Knowledge Networks and Data Sharing
Clinical Paradigm	<p>Updates from industry, FDA, Clinical trial conferences:</p> <p>Next generation trial design (long-term studies, Real World Evidence, Patient Centric endpoints, consortia models, post-marketing)</p>
Strategic Partnerships	<p>Tangible deliverables from recently implemented demonstration cases:</p> <ul style="list-style-type: none"> • NHLBI for Cure Sickle Cell • CZI for COVID genomics
Training Future Scientists and Workforce	<p>Need for education and training programs validated by input from the community, industry, current EDU programs and academic institutions.</p> <p><i>* COVID crisis with slashed fellowships and post-doc funding poses an immediate threat to talent pipeline ("Pandemic darkens postdocs' work and career hopes" Nature September 2020)</i></p>

CIRM Pillars ideally suited for Future Consortia

← *Future Consortia: Learning Network, Acceleration, Efficiency, Hub for Partnerships* →

COVID-19

Alpha Clinics academic & industry trials

Genomics Program *example, CZI MOU*

Sickle Cell
example, NHLBI MOU



Education



Infrastructure



Discovery



Translation



Clinical

Knowledge and Data Networks
(IP and Privacy protection)

CIRM
CALIFORNIA STEM CELL AGENCY

Update on Pathways to Commercialization Concept

Best in Class Investment & Commercialization Partnerships	Facilitate “quality by design” and accelerate project progression	<p>Opportunity to leverage Industry Alliances</p> <hr/> <p>Industry interest in engaging earlier</p>
Attract & Facilitate Economic Development in CA for Regenerative Medicine	Create capacity to address key gating items to commercialization	Public-Private manufacturing partnerships viewed as a promising solution to key gating issues by academic & industry stakeholders

Update on Strategic Concepts to Increase Patient Access

Considerations of Diversity, Equity and Inclusion will be an integral part of the strategy

Patient Navigation Resources	Data Registry and Educational Materials created from output of Research Programs
	Training and Certification program for Patient Navigators and Counselors via EDU programs
	Clinical Infrastructure by Expansion of Clinical Networks in Academia and in the Community via INFR program
	The bidirectional flow of information and interactions between CIRM research programs and the community = CIRM's Communication and Patient Engagement strategy
	Based on "deep dive" and gap analysis, novel funding mechanism for public health research - e.g. social determinants of health, barriers to clinical trial participation and healthcare delivery
	TBD pending input & guidance from Accessibility and Affordability Workgroup
Treatment Access and Coverage*	*Accessibility and Affordability Working Group being formed by ICOC

Update on Operational Excellence Concepts

<p>Recurring RFAs</p>	<p>DISC/TRAN/CLIN (Concept Amendments for ICOC action today) EDU/INFR (first set of concepts will be brought to board early 2021)</p> <p>New RFAs following adoption of Beyond 2020 Strategic Plan</p>
<p>Implement Strategic Themes</p>	<p>CIRM Operations will serve as cable to integrate and standardize approach for:</p> <p>Data Sharing (in Concept Amendments for ICOC action today)</p> <hr/> <p>Integrate and standardize new elements into application, review & tracking:</p> <p>Diversity Equity and Inclusion (in Concept Amendments for ICOC action today)</p>
<p>Additional Funding & Review Formats</p> <p>12/21/20</p>	<p>Renewal applications, Supplemental funding, Planning grants, Targeted RFAs, Infrastructure and Special RFA GWGs</p> <p>Roll out Revised Pillar RFA's (as per Jan-June Plan)</p> <p>New RFAs following adoption of Beyond 2020 Strategic Plan</p>

SOMETHING BETTER THAN HOPE

CIRM Therapeutics & Infrastructure Team Update

Abla A Creasey, PhD
Vice President, Therapeutics & Strategic Infrastructure
December 21, 2020

12/21/20

Therapeutics: 2020 Clinical Portfolio Achievements



Exceeded CIRM 2016-2020 Strategic Goal of 50 NEW Clinical trials

- Current portfolio: **12 CLIN1 & 45 CLIN2** active grants
- 2 received Accelerated FDA RMAT designation
- 1 received Breakthrough designation
- 1 received PRIME designation
- 8 newly launched awards
- 4 CLIN1 awards Filed INDs- 60% filed IND < 18 months
- 3 COVID-19 CLIN2 grants
- 3 Sickle Cell Disease grants with NHLBI

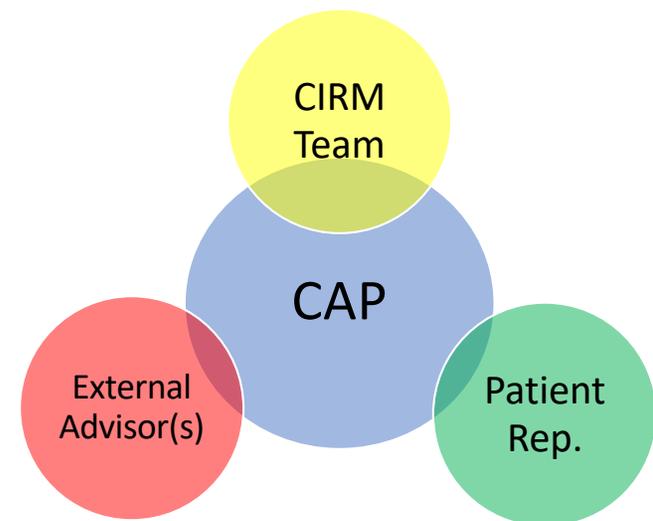


Therapeutics: 2020 Clinical Advisory Panels (CAP)

Goal: To work closely with Project Teams to accelerate development of therapies

Key Opinion Leaders / Advisors participate

- **52 CAP meetings** resulting in strategic solutions/recommendations
 - Targeted Regulatory Advice & FDA Interactions
 - Addressing Manufacturing Challenges
 - Clinical Trial Execution including Enrollment
 - Development Path Delineation & Refinement
 - Partnering Facilitation
- Multiple mini-CAPs for interim updates



2020 CIRM Scientific Publications & Presentations

National Academy of Sciences, July 21, 2020
“CIRM’s Clinical Studies for COVID-19 Treatment” – Dr. Sohel Talib

Received: 24 February 2020 | Accepted: 18 May 2020
DOI: 10.1002/sctm.20-0079

PERSPECTIVES



Enabling allogeneic therapies: CIRM-funded strategies for immune tolerance and immune evasion

Lisa C. Kadyk | Ross M. Okamura | Sohel Talib

California Department of Health, September 28, 2020
“Advancing World Class Science and Patient Engagement: CIRM’s Sickle Cell Disease Portfolio” – Dr. Sohel Talib

Received: 6 February 2020 | Accepted: 30 May 2020
DOI: 10.1002/sctm.20-0055

PERSPECTIVES



CIRM tools and technologies: Breaking bottlenecks to the development of stem cell therapies

Lila R. Collins | Kelly A. Shepard

> Stem Cells Transl Med. 2020 May;9(5):547-553. doi: 10.1002/sctm.19-0377. Epub 2020 Feb 10.

Regulated, reliable, and reputable: Protect patients with uniform standards for stem cell treatments

Geoffrey P Lomax¹, Art Torres¹, Maria T Millan¹

Received: 3 November 2019 | Accepted: 2 January 2020
DOI: 10.1002/sctm.19-0375

PERSPECTIVES



Unleashing the cure: Overcoming persistent obstacles in the translation and expanded use of hematopoietic stem cell-based therapies

Sohel Talib | Kelly A. Shepard

CELL & GENE THERAPY INSIGHTS

Investor Insight

COMMENTARY

Boldly De-Risking Development of Impactful Cell and Gene Therapies: The California Stem Cell Agency’s \$3B Funding Model

Shyam Patel, Sohel Talib & Maria T. Millan



Journal | Articles



Actions

STEM CELLS Translational Medicine / Volume 9, Issue 8

PERSPECTIVES | Open Access | CC BY

Two cancer stem cell-targeted therapies in clinical trials as viewed from the standpoint of the cancer stem cell model

Ingrid W. Caras

First published: 12 April 2020

2020 Public Reports from CIRM Clinical Programs



December 14, 2020

Graphite Bio Receives IND Clearance to Initiate Clinical Trial for Next-Generation Gene Editing Therapy GPH101 in Sickle Cell Disease



Volume 26, Issue 3, Supplement, March 2020, Pages S88-S89

119

Early Outcome of a Phase I/II Clinical Trial (NCT03538899) of Gene-Corrected Autologous CD34+ Hematopoietic Cells and Low-Exposure Busulfan in Newly Diagnosed Patients with Artemis-Deficient Severe Combined Immunodeficiency (ART-SCID)

Morton J. Cowan MD^{1,2}, Jason Yu PhD¹, Janelle Facchino PNP⁴, Shivali Chag MS², Carol Fraser-Browne¹, Janel Long-Boyle PharmD, PhD⁵, Misako Kawahara³, Ukina Sanford MS¹, Jess Oh⁶, Suan Teoh⁶, Divya Punwani PhD³, Jasmeen Dara MD³, Christopher C. Dvorak MD¹, Lori Broderick MD, PhD⁷, Diana Hu MD⁴, Holly K. Miller DO⁸, Aleksandra Petrovic MD¹⁰, Harry L. Malech MD¹¹, Jennifer Puck MD^{1,2}



Source: Oncernal Therapeutics
December 07, 2020 08:00 ET

Oncernal Therapeutics Announces Presentation of Interim Phase 1/2 Data Update for Cirmtuzumab in Combination with Ibrutinib at ASH 2020 Virtual Annual Meeting

12/21/20



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330 The First-in-Class Anti-CD47 Antibody Magrolimab Combined with Azacitidine Is Well-Tolerated and Effective in AML Patients: Phase 1b Results

Program: Oral and Poster Abstracts
Type: Oral
Session: 613. Acute Myeloid Leukemia: Novel Therapies and Treatment Approaches
Hematology Disease Topics & Pathways: antibodies, Biological, AML, Leukemia, Diseases, Therapies, Myeloid Malignancies, stem cells

Sunday, December 6, 2020: 9:30 AM

David A. Sallman, MD¹, Adam S. Asch, MD², Suman Kambhampati, MD³, Monzr M. Al Malki, MD⁴, Joshua F. Zeidner, MD⁵, William Donnellan, MD⁶, Daniel J. Lee, MD⁷, Paresht Vyas, MRCP, FRCP, FRCPath⁸, Deepa Jeyakumar, MD⁹, Gabriel N. Mannis, MD¹⁰, Tiffany N Tanaka, MD¹¹, Wanxing Chai-Ho, MD¹², Richard A. Larson, MD¹³, Andrew R. Whiteley, MD¹⁴, Guido Marcucci, MD¹⁵, Rami S. Komrokji, MD¹⁶, Guillermo Garcia-Manero, MD¹⁵, Joanna Van Elk¹⁶, Ming Lin, PhD¹⁶, Roy Maute, PhD¹⁶, Jens-Peter Volkmer, MD¹⁶, Chris H. Takimoto, MD, PhD¹⁶, Mark P. Chao, MD, PhD¹⁶ and Naval Daver, MD¹⁵



Celularity Doses First Patient in Clinical Trial Evaluating CYNK-001 in COVID-19 Patients

By Celularity Inc in COVID, Press Releases



ABOUT OUR APPROACH PIPELINE PARTNERING CAREERS INVESTOR RELATIONS

Investor Relations

Press Release

Mustang Bio Announces Rare Pediatric Disease Designation for MB-107 for the Treatment of X-linked Severe Combined Immunodeficiency

Company Release - 08/17/2020 ET



2020 Public Reports from CIRM Clinical Programs



**News Release
Details**

[« Back](#)
Rocket Pharmaceuticals Presents Positive Updates on FA and LAD-I Gene Therapy Programs at the 23rd Annual Meeting of the American Society of Gene and Cell Therapy

May 12, 2020 |



ViaCyte to Present Preliminary PEC-Direct Clinical Data at Cell & Gene Meeting on the Mesa



MENU ≡

- AVR-RD-04 for cystinosis: Functional and clinical improvements for the first patient at 1 year; third patient in the trial dosed



Wexner Medical Center Performs First Gene Therapy Brain Infusion For Parkinson's Disease

[Home](#) / [Media](#) / [Press Releases](#)

September 3, 2020

Press Release

Medeor Therapeutics' Transplant Immune Tolerance Therapy Receives Regenerative Medicine Advanced Therapy Designation from FDA

Angiocrine Bioscience Announces Oral Presentation of AB-205 Data during the 62nd Annual Meeting of the American Society of Hematology (ASH)

Published: Dec 04, 2020

12/21/20



Conferences



- CIRM Grantee Meeting
- Alpha Stem Cell Clinics Symposium
- CIRM Bridges Meeting (Kent Fitzgerald)

CIRM 2020 Grantee Meeting

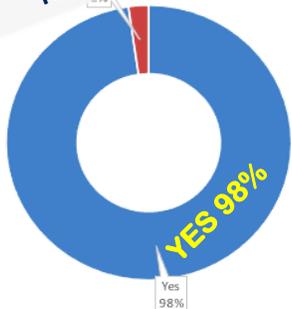


September 14-15, 2020

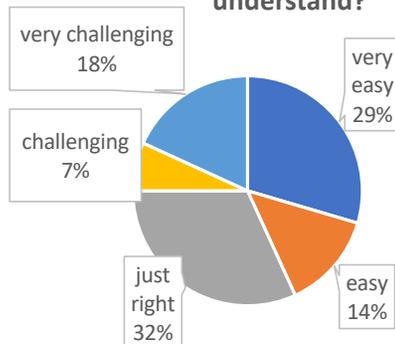
Hosted by Sanford Stem Cell Clinical at UC San Diego, UC Irvine, and CIRM



Did we increase your understanding of stem cell research?



Were the presentations challenging for you to understand?



Sharing the latest in stem cell research conducted in California - progress, obstacles and the future

- 39 Speakers: 18 Female & 21 Male
- 743 Registrants over Two Days

Audience composed of the general public, scientists and patient advocates

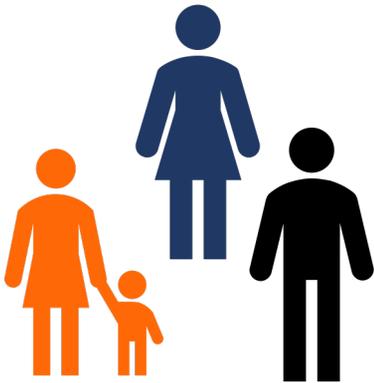
2020 CIRM Alpha Clinics Symposium



UC DAVIS HEALTH | Alpha Stem Cell Clinic

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CALIFORNIA STEM CELL AGENCY

Alpha Stem Cell Clinic Network Virtual Symposium



376 Registrants

- Five Sessions featuring clinical trials within the Network
- Patients and their families describing their journey in these clinical trials
- Dual panel on COVID-19 clinical trials and Diversity, Equity and Inclusion in clinical trials
- Complete archive at:
<https://www.cirm.ca.gov/patients/alpha-clinics-network/alpha-clinics-news>

SOMETHING BETTER THAN HOPE

Update on Discovery, Translation and Education Programs

Kent Fitzgerald, Ph.D.

Director, Discovery & Translational Science

Dec. 21, 2020

12/21/20

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Education Program: 2020 Achievements

14 active EDUC2 programs/institutions

- 103 current interns (total of 1,603)
- ~200 mentors across 60 different host academic, nonprofit and biotech organizations



EDUCATION

CIRM Bridges Meeting (July 6-8, 2020) Highlights:

Rapid response by organizers to implement an online meeting format

- Topic Sessions: Eye Disease, Colon Cancer, Parkinson Disease plus one special COVID-19 session
 - structured to feature basic scientists, clinical scientists, and patients
- 5 virtual poster sessions
- 220 online participants



Discovery Program: 2020 Achievements

- 30 discovery programs launched (including 12 COVID programs)
- 26 programs concluded or expected to conclude by year end
- 6 programs advancing to the next stage of development
 - Kuo, Hyper-IgM; Nicholas, epilepsy
 - 3 spin-outs
 - 1 Tools and Technology
- 7 discovery awards progressed to achieve next stage funding



Translational Program: 2020 Achievements

- 5 TRAN programs launched (4 traditional and 1 TRAN1COVID19)
- 1 project completed (23 ongoing TRAN projects)
- 3 pre-IND interactions with the FDA conducted signaling an advance toward IND enabling studies



TRANSLATION

Translational Advisory Panels (TAP)

- Purpose: To work with Project Team to accelerate successful development of a therapy for patients
- 11 TAP meetings resulting in strategic solutions/recommendations
 - cGMP Process Development Challenges Resolved
 - Pre-clinical Study Design Optimized
 - Targeted Regulatory Advice
 - Regulatory Submission Review
 - Development Path Refined
 - Partnering Facilitated



12/21/20

COVID-19 Special Call



CIRM PIs that saw the immediate need brought on by the pandemic and were able to rapidly pivot their own research to address this tremendous need.

Program announced: April 10, 2020 & Reviewed April 21, 2020

First projects launched: June 1, 2020

15 COVID-19 directed project funded (1 DISC1, 12 DISC2, 1 TRAN1, 1 DISC2P)

Summary of Early Stage COVID Projects:

- Candidate Discovery for Therapeutics
 - Stem cell derived lung organoid models for the discovery of drugs that could be fast tracked to tackle SARSCoV viral lung infection. Gomperts (UCLA), Ichida (USC) & Snyder (Sanford Burnham SD)
 - Elucidating T cell immune mechanisms against the virus. Crooks (UCLA), and Wong (Stanford).
 - Treatment of damage resulting from viral infection or ventilator use. Christman (UCSD) and Blau (Stanford)
- Translational stage program for a SARS-CoV-2 anti-viral therapy (Arumugaswami, UCLA)
- Tools to better target antisense therapy to alveolar cells (Dowdy, UCSD) and discovery and screening tools for COVID therapies (Healy, Berkeley)

SOMETHING BETTER THAN HOPE

Update on Business Development & CIRM's Industry Alliance Program

Shyam Patel, PhD
Director, BD & Alliance Management
December 21, 2020

12/21/20

CIRM Funding Attracts Industry Investment

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

Over 50% of CIRM-funded Clinical Programs are partnered with Industry.

Three CIRM-funded Companies issued IPOs.

CIRM funding of academic projects has enabled the spinout of 45 companies (5 in 2020).

Industry Partnership
>\$13 Billion

2020 | \$ 9.6B (YTD)

2019 | \$1.5B

2018 | \$1.3B

2017 | \$389M

2016 | \$153M

2015 | \$45.5M

2014 | \$37.5M

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Highlighted Academic Spinouts

Public/Acquired



Forty Seven, Inc.



Venture Funded/Biopharma Partnered



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2020: Highlighted Industry Partnering Events

Forty Seven, Inc.	Cancer Immunotherapy	Acquired by Gilead Sciences for \$4.9B
	Cancer Immunotherapy	Acquired by Merck for \$2.75B
	Cell Immunotherapies for Cancer	\$204.8M Initial Public Offering
	Cell Therapy for Retinal Diseases	\$252M Ex-US License to Santen Pharmaceutical
	Gene Therapy for Parkinson's Disease	Acquired by AskBio, a Bayer Company
	Gene Therapies for Rare Diseases	\$299M Public Offering
 12/21/20	Cell Therapies for Parkinson's Disease	Secured \$75M Series A Funding



INDUSTRY
ALLIANCE
PROGRAM

CIRM's Industry Alliance Program (IAP): A unique opportunity for the industry to partner with CIRM in accelerating clinical and preclinical stem cell, gene and regenerative medicine therapy programs to market.

Launch Partners (2018)



PANACEA VENTURE
HEALTHCARE



BlueRock
Therapeutics

Joined in 2019



Joined in 2020



Past 18 Months: Over 50 One-on-One Partnership Interactions between IAP Members and CIRM Grantees

12/21/20

IAP Joint Partners Meeting December 11, 2020

Meeting Agenda:

1. CIRM Update
2. CIRM Portfolio Presentations (3)
3. Industry Partner Feedback Session

Summary of Industry Partner Feedback:

- Increase frequency of CIRM updates and CIRM portfolio interactions.
- Industry partners are eager to support early innovators and early-stage R&D projects with expert advice, capital and resources.
- Industry partners are developing unique models to address manufacturing challenges; they envision a critical role for public-private collaborations.