DRAFT FOR REVIEW ONLY

Real Life™

2022–2026

5-Year Strategic Plan

California Institute for Regenerative Medicine

CIRM
CALIFORNIA'S STEM CELL AGENCY

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Evie Padilla Vaccaro

Introduction

CIRM
CALIFORNIA'S STEM CELL AGENCY

The establishment of the California Institute for Regenerative Medicine (CIRM) under Proposition 71 in 2004 marked a historic moment for the advancement of a new field in science and an investment in a new class of potentially curative regenerative medicine approaches.

Since its launch, CIRM has been a leader in growing the stem cell and regenerative medicine field while keeping the needs of patients at the core of its mission and maintaining a partnership with the patient community.

CIRM has established a strong track record for strategic investments in five pillars—infrastructure, education, discovery, translational and clinical research. It has distinguished itself from other funding agencies in the level of support and funding for the so called translational research "valley of death," the stage where scientific findings need further work to be developed into potential therapies.

CIRM, as a collaborative partner, de-risks programs by choosing projects that have met high scientific rigor through its highly refined peer review process and funding these "high risk but high reward" programs when others are not yet ready to fund them.

CIRM has built a vibrant regenerative medicine ecosystem in California, funding the education and training of its future resource, creating engagement and investment opportunities through industry engagement, and by addressing infrastructure gaps that hinder the progress of the field.

CIRM as the patient-centric funder:

- Advanced stem cell research and therapy development for more than **75 diseases**.
- Funded **75+ clinical trials**, from first-in-human to pivotal phase 3, with 3,200+ patients enrolled.
- Engaged **patient advocates at every step of the CIRM process** from Board representation, to review and approval of grant applications to collaborative advisory panels on clinical trial projects.
- Helped **cure over 40 children** of fatal immunological disorders with gene-modified cell therapies.

Patient-Centric Funder

Ronnie Priyank

When Ronnie was born, he seemed like a happy, healthy baby. But within a few days, a newborn screening test diagnosed him with X-linked SCID, a rare immune disorder that was often fatal within two years. Fortunately, doctors told his parents about a clinical trial, funded by CIRM, run by UC San Francisco and St. Jude. Doctors took some of Ronnie's own blood stem cells and, in the lab, corrected the genetic mutation that caused the condition. They then gave him a mild dose of chemotherapy, to clear space in his bone marrow, for the corrected cells to be placed and to grow. Over the next few months, the blood stem cells created a new blood supply and repaired Ronnie's immune system. He is now a happy healthy three-year-old boy who loves going to school with other children.

This approach, as well as others funded by CIRM for various types of SCID, are currently being tested as investigational therapies in clinical trials to demonstrate both safety and efficacy across a large patient population.

CIRM as the seeder of innovative stem cell biology and translational research:

- Supported **1,000+ projects at 70 institutions** across California.
- Funded **12 world class stem cell research facilities** at California's leading academic research institutions.
- Overcame federal funding restrictions on hESC research by building **17 shared research laboratories** and by pioneering the derivation of new hESC lines.
- Facilitated over **3,000** peer-reviewed publications of **scientific and medical discoveries**.
- Built the **world's largest iPSC research repository with over 2,600 stem cell lines** for modeling diseases such as Alzheimer's disease, neurodevelopmental disorders, and cardiomyopathies.
- Enabled **innovative discovery and translational tools** such as cell and animal models, assays, and manufacturing processes that have contributed to more than 300 publications, 63 inventions and 13 patents.
- Spurred creation of **novel genomic datasets and bioinformatics tools for stem cell research**, including some of the earliest single-cell gene expression atlases of the human body.

Innovative Researcher

Lili Yang, PhD, Associate Professor, UCLA

For the last eight years, CIRM has supported the work of Dr. Lili Yang's laboratory in generating invariant Natural Killer T cells (iNKT) with five different grants spanning from the initial identification of the technology that produced the therapeutic to translation stage development that culminated in a formal pre-IND meeting with FDA. Dr. Yang has used the iNKT platform to develop both autologous and off-the-shelf allogenic anti-cancer therapeutics designed to target blood cell cancers. Her work has been viewed as successful enough to be the basis of a start-up company (AppiaBio) that recently announced a collaboration with Kite Pharma in order to help develop and commercialize this promising technology. Dr. Yang's story captures CIRM's commitment to supporting innovative research that paves the way for development of next-generation therapies.

CIRM as the accelerator for therapy development[1]:

- Funded patient-centered clinical trials with the highest standards of care by establishing **5 Alpha Stem Cell Clinics** that have supported 100+ clinical trials across the state.
- Supported the **pioneering US clinical trials of hESC-derived cell therapies** for spinal cord injury, diabetes, and age-related macular degeneration.
- Enabled CIRM programs to qualify for **15% of the regenerative medicine advanced therapy designation** (RMAT) expedited pathway designation issued by the FDA
- Accelerated late-stage preclinical development with **73% of pre-clinical programs achieving FDA permission to initiate clinical trials within 2 years.**
- Supported the **progression of 75 programs into therapy development** via successive CIRM awards, including 20 candidates that progressed from discovery or early preclinical development into clinical trials.

Therapy Accelerator

Joseph Wu, MD, PhD, Professor of Medicine, Stanford University

As the recipient of multiple CIRM awards, Dr. Joseph Wu has been extensively studying key safety aspects of hESCs for many years. His work has produced high-impact publications and his observation that pluripotent stem cells express novel immunogenic antigens shared by tumors evolved into a cancer vaccine technology now being developed by Khloris Biosciences, a biotechnology company spun out from Dr. Wu's lab, in partnership with Leaps by Bayer. Additionally, using his basic biology and pre-clinical findings, and in collaboration with City of Hope and funded by CIRM, Dr. Wu developed a robust, GMP-compatible, scalable process to produce hESC-derived cardiomyocytes for clinical use after ischemic heart disease. In partnership with CIRM, Dr. Wu has launched the first-in-US clinical trial for this therapy. His CIRM-funded work has also led to the development of hiPSC-derived cardiomyocytes with Khloris Biosciences as well as a collaboration with the University of Goettingen's Dr. Wolfram Zimmermann for the potential clinical use of this technology as a patch. Dr. Wu's story captures how CIRM researchers leverage CIRM support to translate basic biological discoveries into potentially transformative therapeutic candidates for devastating diseases.

CIRM as the ecosystem builder:

Trained over
3,000
students and scholars
to become the future workforce of regenerative medicine.

Stimulated the CA economy with
$10.7B
of gross output and
56,000
new FTE jobs created during the 2004-2018 period.[2]

Positioned CIRM-funded projects to attract
$18B+
of industry funding.

Ecosystem Builder

SPARK Program

To train the next generation of stem cell scientists, CIRM created the SPARK (Summer Program to Accelerate Regenerative Medicine Knowledge) program to give high-school students from diverse backgrounds a chance to gain hands-on training in stem cell research at some of the leading research institutes in California. SPARK specifically selects students who represent the diversity of California's population, particularly those who might not otherwise have opportunities to partake in research internships due to socioeconomic constraints. To date, 482 students have been trained by the SPARK program.

Some trainees are still in high school but of 171 alumni who reported college attendance:

- *40% attended/are attending a UC.*
- *26% attending another CA school (Stanford, Caltech, CSU).*
- *33% attend schools outside CA (Yale, Columbia, Harvard, Johns Hopkins, Duke, Princeton, etc.).*
- *Of 141 declared majors: 96% biology and other STEM-related fields.*

CIRM has come a long way…

but this is just the start of fully realizing the potential of what was made possible and set in motion by Proposition 71. In recent years, we have already started to see examples of where regenerative medicine approaches have the ability to transform the lives of patients. CIRM's clinical trials using gene therapy to correct various forms of inherited immune disease, success by others in gene therapy for spinal muscular atrophy and for inherited blindness, and the explosion of CAR-T therapies for refractory and deadly cancers have marked the beginning of a new era.

To realize the full potential of regenerative medicine for society, a significant amount is left to be done in basic and translational research and in the downstream challenges of delivering these promising treatments to patients with debilitating and fatal conditions. In addition, the continued success of the field will create more challenges—challenges in commercialization, equitable access to treatments, healthcare delivery models and payment models to support this new class of therapies.

The passage of Proposition 14 in 2020 has positioned CIRM to continue to accelerate research, strengthen the ecosystem and drive innovative, real world solutions to deliver resulting transformative treatments to a diverse community of patients in need and to do so in an equitable manner.

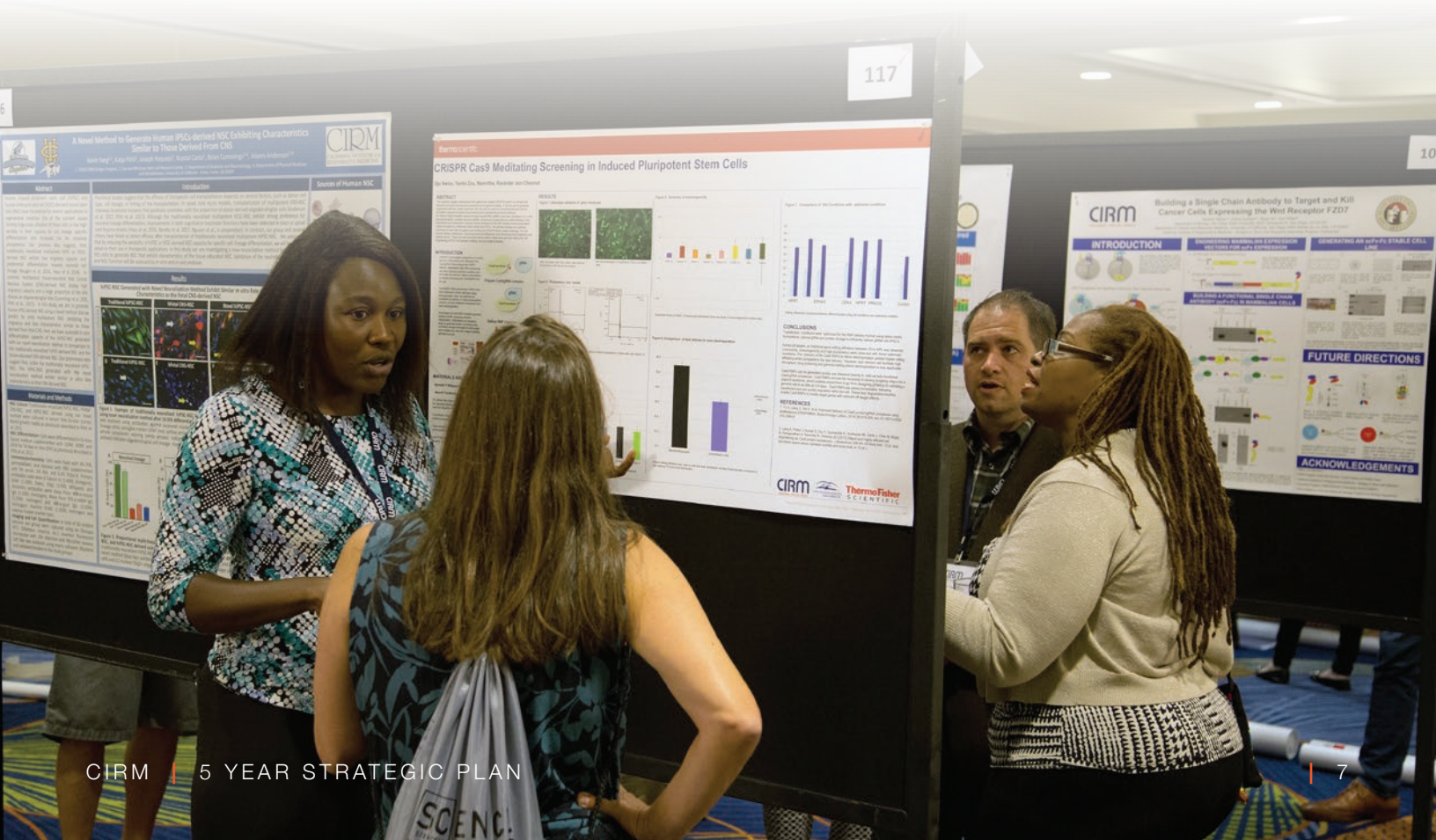
CIRM has expanded its mission statement to reflect the next phase of the Institute. CIRM will leverage its proven patient-centric funding and partnership model to **accelerate** world class science into **transformative** regenerative medicine treatments while committing to **deliver** these treatments in an equitable fashion to a diverse California and world. The strategy for accomplishing this bold, expanded mission will involve a culture shift in how we coordinate our scientific endeavors. It will involve the development of novel healthcare delivery models and the growth of a skilled workforce.

CIRM
CALIFORNIA'S STEM CELL AGENCY

MISSION STATEMENT

Accelerating stem cell treatments to patients with unmet medical needs.

Accelerating world class science to deliver transformative regenerative medicine treatments to a diverse California and worldwide in an equitable manner.



Since its inception, CIRM's mission and strategic goals have stayed true to the spirit of Proposition 71 by striving to rapidly advance stem cell and regenerative medicine technologies toward treatments and cures for patients' unmet medical needs.

In 2006, CIRM's first strategic plan and its mission statement reflected the challenges and opportunities in the emerging field of stem cell and regenerative medicine. The seminal paper on human induced pluripotent stem cells had yet to be published. Second generation CAR-T cell technology was showing promise in preclinical models but had not yet demonstrated its clinical potential. The 2006 mission statement thus focused on the need to accelerate research of stem cell and regenerative medicine technologies while maintaining the highest medical and ethical standards.

In 2016, as CIRM issued its final strategic plan of the Proposition 71 era, the field had advanced considerably after several critical clinical milestones. CAR-T cells had demonstrated preliminary clinical safety and efficacy for blood cancers. Gene therapies and gene-modified cell therapies had showed clinical benefit for rare monogenetic diseases. Pluripotent Stem Cell-based cell therapies had progressed to clinical studies. CIRM's mission statement was thus modified to capture the urgency of accelerating translational research and propelling more promising therapies into clinical development. The re-stated mission statement defined the 2016 strategic plan's goals of accelerating translational research and developing the resources to ultimately support 50 new clinical trials in 5 years.

Now in 2021, as CIRM sets its vision for the Proposition 14 era, its mission and strategic goals must reflect the current state of regenerative medicine and address the next decade's challenges and opportunities. Today, the clinical benefit of stem cells and regenerative medicine continues to be validated by the hundreds of ongoing clinical trials and by the real world use of approved therapies. New technologies such as CRISPR gene editing are showing clinical promises in genetic blood, eye and neurological diseases as well as in cancer. Given the initial clinical success in rare blood diseases and oncology, stem cell and regenerative medicine technologies are being aimed at a broader range of diseases from rare monogenetic diseases to neurodegeneration, diabetes, and heart disease. As the field advances rapidly, it is imperative that the promise of regenerative medicine is realized as accessible, transformative, real-life therapies for patients across a diverse California and worldwide.

With this mission as its “north star,” CIRM has set out a

new strategic plan

that seeks to address the challenges and opportunities presented by the growing field of regenerative medicine.

The strategy is organized into **three major themes**:

Advance

World Class Science

Deliver

Real World Solutions

Provide

Opportunity for All

Real Life™

The challenges, opportunities, and measurable 5-year goals related to each strategic theme are discussed below.

Advance World Class Science

To advance world class science, CIRM will leverage collective scientific knowledge to inspire collaborative research that addresses Californians' unmet medical needs.

5-year Strategic Goals:

- Develop next-generation **technology competency hubs** that broadly empower and connect California's research ecosystem
- Build **knowledge networks** that foster and advance novel discovery, translational and clinical research approaches

The field of regenerative medicine is advancing rapidly, driven by novel research tools and technologies that generate terabytes of data on human biology, but has to date resulted in few demonstrably effective treatments for devastating diseases. This is particularly true for diseases of the central nervous system where the complex biology underpinning neuropsychiatric, neurodevelopmental, and neurodegenerative diseases is still coming into focus and disease-modifying therapies remain elusive. Several factors contribute to the limited scientific advancement in these areas, including: 1) Lack of attention and financial support (from non-profit and industry sectors) for high-risk/high-reward research and therapy development, particularly in disease indications that are not commercially viable (i.e., rare diseases) or are complex (i.e., CNS-related diseases), and 2) The siloed nature of biomedical research and development. This strategic plan will address these key issues.

High-Risk/High-Reward Research Projects. CIRM is committed to maintaining and augmenting high-risk/high-reward projects, including rare diseases and neurological disorders. CIRM's unique funding partnership model has provided predictable, reliable, and progressive funding for projects that were considered too risky in their discovery stages for financial support from governmental institutions or industry[3]. To date:

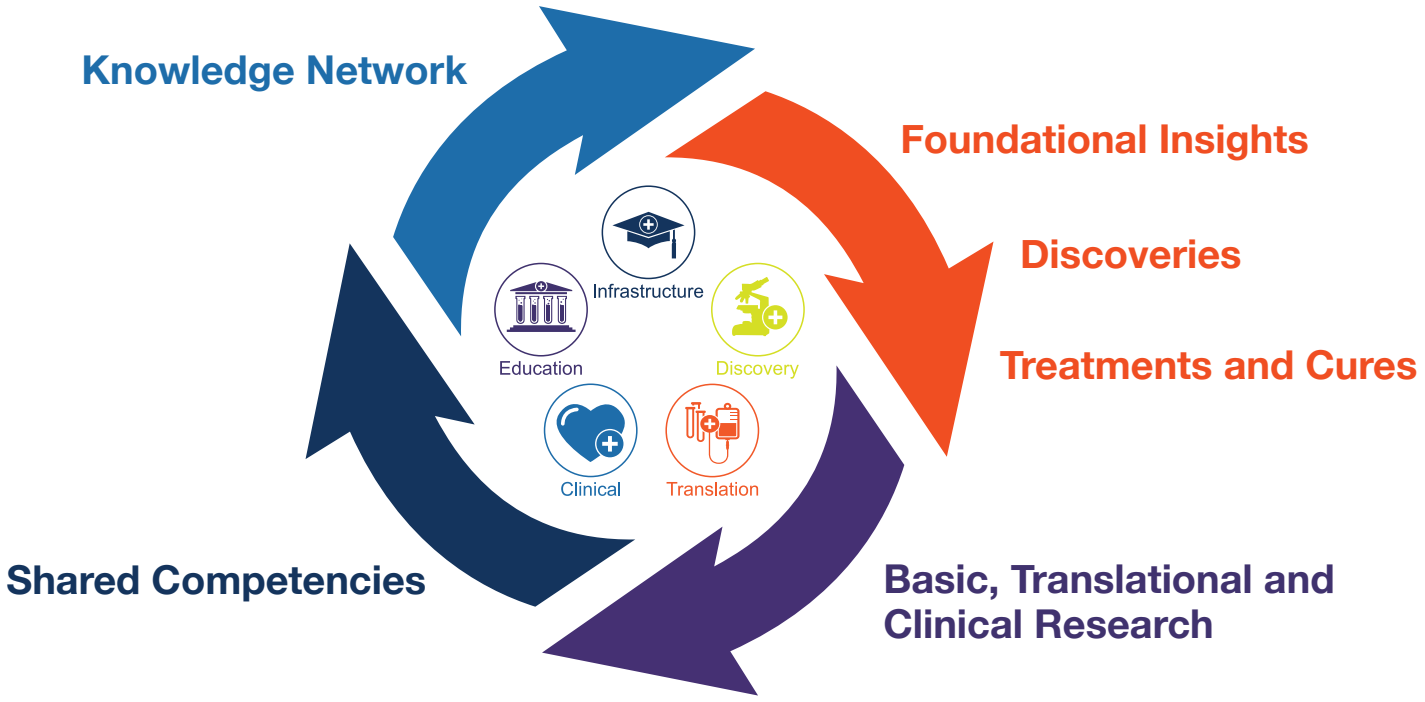
- In addition to the 76 CIRM-funded clinical trials, CIRM funding of preclinical projects has enabled an additional 31 clinical trials[4].
- Nearly 12% of CIRM's clinical funding comprises high-risk/high-reward stem cell and gene therapy approaches for rare diseases.
- Almost a quarter of CIRM's total funding has focused on neurological disorders[5] and 14% of its clinical portfolio comprises CNS diseases.
- CIRM's hiPSC repository has enabled studies in psychiatric diseases: Broad Institute investigators have identified lines with extreme high and low polygenic risk scores for schizophrenia[6].

In this strategic plan, and in line with the recommendations of the Strategic Scientific Advisory Panel[7], CIRM will maintain and augment this commitment in 2 ways: 1) Continue the funding mechanisms through the existing pillar programs; 2) Design infrastructure that organizes and democratizes data through knowledge networks and accelerates shared usage of specialized technologies through competency hubs. This strategy will be deployed within the broad CIRM funding programs, but will initially be designed to enable a consortium approach to CNS research, including neuropsychiatric and neurodevelopmental disorders[8].

Culture of Collaboration. CIRM is committed to develop a systematic approach that fosters "team-science." Scientific research and therapy development has always been driven by small teams or targeted collaborations between research labs. On the other end of the spectrum, large-scale collaborative efforts driven by public and private stakeholders tend to be fewer in number but have demonstrated success stories; the advent of cancer immunotherapies or the recent rapid development of COVID-19 vaccines being two of the more prominent examples. Despite the prevalence of small and large-scale collaborative efforts, the biomedical research enterprise still functions in silos where valuable data, resources and expertise are selectively shared.

In recent years, there has been a paradigm shift underway in this culture of biomedical research toward one of greater data and resource sharing and broader coordination of research activities. While data sharing is not a new concept by any means, the current patchwork of public and private data repositories has several limitations including lack of data standardization, limited interoperability and lack of analytical toolkits. These limitations make it difficult to access, combine and analyze the shared datasets for meaningful research insights. To address these limitations, the NIH and other institutions and organizations have established data sharing policies and developed collaborative resource sharing. CIRM will promote a culture of collaborative research by investing in the research and technology infrastructure to advance and facilitate sharing of unique resources (see section on competency hubs below) and meaningful CIRM-funded research data (see section on knowledge networks below).

Investments in technology competency hubs and knowledge networks will advance collaborative world class scientific research and fuel discoveries that could lead to translational and clinical candidates. This model would also support the potential for "reverse translation," where new knowledge gained from late-stage translational and clinical research could be addressed in discovery research which, in turn, could result in new translational and clinical programs.



5-Year Strategic Goals

Develop next-generation technology competency hubs that broadly empower and connect California's research ecosystem

Scientific progress relies on revolutionary and interdisciplinary breakthroughs in technology. Cutting-edge methodologies such as CRISPR gene editing, human cell modeling of disease, machine learning, AI, and others could significantly enhance scientific discovery and accelerate therapy development. However, practical utilization of these innovations often requires upfront investment in technologies, iterative development and validation, standardization of protocols, and specialization in training and expertise. These barriers limit research access and can delay maturation and widespread adoption of the technology platform. Individual academic institutions address these barriers with centralized core research facilities that make specialized equipment and provide accessible expertise and training broadly to the institution's research labs and courses.[9] Early in its history under Proposition 71, CIRM had established 17 shared research laboratories as core facilities for stem cell research and training, many of which are still operational today. Proposition 14 re-establishes and expands the shared laboratories programs.

CIRM will build on the shared laboratories model to develop competency hubs that will accelerate hypothesis-driven research, translational and clinical development of regenerative medicine therapies and workforce development in CIRM's pillar programs. The competency hubs will concentrate and network domain-specific expertise and innovation to develop, validate and broadly share unique technology-driven competencies. Examples of competency hubs could include human cell models of disease[10], and/or gene editing resources. The competency hubs will offer expertise in novel technologies, trained personnel, training courses, equipment, and standardization of workflows to broadly serve three functions: (1) innovate and improve on[11] the technology core competencies to augment their impact for CA researchers and to further support regenerative medicine research and development; (2) provide broad access to the shared resources, training, and protocols; and (3) support and facilitate collaborative research approaches across CIRM's discovery, translational and clinical pillars. Other forms of competency hubs will be incorporated into existing or planned CIRM strategic infrastructure such as Alpha Stem Cell Clinics, Community Care Centers, and the California Manufacturing Network (Explained further in Theme 2, Deliver Real World Solutions).

"Updating the technological capabilities of existing shared labs and stimulating partnerships with institutions that currently lack such expertise will create and strengthen close collaborations and generate a robust network of therapy discovery and delivery."

—Lawrence Goldstein, PhD, ICOC Board Member

Given the rapidly growing and evolving nature of the regenerative medicine field, a critical function of the competency hubs will be to continuously innovate, develop and validate the core technologies in collaboration with the users and other competency hubs in the network. The competency hubs will provide inter-institutional access to the technology by sharing facilities, training, equipment, materials, protocols, and/or expertise. For example, a disease modeling competency hub could provide access to facilities, equipment and training programs for deriving or differentiating cell lines or it could share the differentiated cells and appropriate protocols with

researchers across the state. The competency hubs will facilitate collaborative research approaches by adapting their technology and/or developing specialized data and resource sharing mechanisms to facilitate the needs of the CIRM-funded collaborative projects. The competency hubs will also constitute part of the CIRM collaborative ecosystem making all their data available through the CIRM data infrastructure hub, also known as CIRM Knowledge Platform, which is explained further below.

Some competency hubs could serve as a workforce training microcosm for local and neighboring institutions. Most California state universities and community colleges have neither the financial nor experiential bandwidth for innovative research, but they may harbor a potential diverse future workforce who could learn these techniques and utilize the technology platforms for small-scale research. CIRM's network of competency hubs will expand geographic access to diverse communities and provide these institutions with a unique opportunity of exposure to state-of-the-art platforms.

Shared Stem Cell Laboratory at UCLA

Success Stories: First Generation Shared Research Laboratories

Under Proposition 71, a total of 17 Shared Research Laboratory grants were awarded to academic and non-profit research institutes to provide dedicated laboratory space that was free of NIH support and equipped to grow and maintain hESCs, served as a shared resource with available core equipment and trained personnel, and in some cases, also provided specialized, hands-on training courses. Shared Labs were available not only to stem cell scientists at the grantee institution but also to those from nearby institutions without such facilities. These dedicated, common laboratories encouraged optimal sharing among individual investigators, research groups and departments to foster a collaborative, multidisciplinary research environment, and promote cost effectiveness. Many of these laboratories have sustained their activities beyond CIRM funding through either fee-for-service contracts or other funding mechanisms and some have expanded their services. For instance, UCLA's Shared Lab includes fully equipped GMP-GTP-compliant labs and USC's space contains core facilities for FACS, biological imaging, therapeutic screening, and tissue culture. In this Plan, CIRM seeks to expand the Shared Lab model by creating networks of specialized and collaborative competency hubs that offer knowledge and best practices in innovative, next-generation technologies and cell and gene therapy development.

5-Year Strategic Goals

Build knowledge networks that foster and advance novel discovery, translational and clinical research approaches

In recent years, funding agencies, publishers, foundations, and academic institutions have adopted more robust data management and data sharing policies. Even with these attempts, however, there remains a great deal of ambiguity around how and what to share, how to meet data sharing requirements and how to harmonize data across the diversity of public and private repositories, all of which significantly limit data usability, scientific productivity, and clinical relevance.

"Making such data sharing and analysis across CIRM projects operational and widely accessible would leverage CIRM investments, serving the biomedical research enterprise broadly."

– Keith Yamamoto, PhD, ICOC Board Member

CIRM will build knowledge networks that facilitate sharing of CIRM-funded data, leverage high-value external datasets and build robust analytical tools to maximize the real world impact of CIRM-funded research. To do this, CIRM will first foster a culture of open science. CIRM will clearly define its own requirements and incentives for well-developed data management and sharing plans in CIRM-funded projects; it will coordinate with other funding agencies, publishers, and California academic institutions to harmonize, facilitate and reward effective data sharing practices. It can network on the one hand with publishing groups to harmonize open science policies and incentivize consortium authorship models, and with funding agencies and institutions on the other hand to build professional reward systems for excellent team science contributions. This multi-faceted approach will generate a healthy ecosystem in which team science is incentivized and the appropriate resources are deployed to achieve this goal[12].

The initial implementation of knowledge networks will focus on accelerating collaborative CNS research approaches[13] that could benefit the study of neurological diseases, including psychiatric disorders. The CIRM knowledge network will facilitate effective management, standardization, sharing and analysis of CIRM-funded research data[14]. The network will address the needs of the research community including basic biology researchers, translational researchers, computational biologists, and clinicians on relevant data types, sharing methodologies and best practices, data governance policies and analytical needs. Data types will include a variety of omics datasets from CIRM-funded research projects and CIRM-funded competency hubs.

To fully leverage these data towards better understanding of brain and CNS diseases and the development of transformative therapies, CIRM will partner with funding agencies, disease foundations and research institutions to enable interoperability and access between CIRM and external neuroscience knowledge networks.

Deliver Real World Solutions

CIRM will overcome critical bottlenecks to accelerate approval of therapies for all patients.

5-year Strategic Goals:

- **Optimize CIRM's clinical trial funding partnership** model to advance more therapies to FDA marketing approval
- **Overcome manufacturing hurdles** for the delivery of regenerative medicine therapies by building a public-private manufacturing partnership network
- **Expand Alpha Clinics and create Community Care Centers of Excellence** that support diverse patient participation in the rapidly maturing regenerative medicine landscape

As the regenerative medicine field matures, more programs are making their way toward potential FDA marketing approval. The pathway from early discovery to commercialization for new therapies, especially those in the regenerative medicine space, is lengthy and expensive. While FDA regenerative medicine therapy approvals are steadily increasing, the number of approved cell and gene therapies today are limited[15]. Recent years have seen the approvals of pioneering cell and gene therapies including CAR-T cell therapies for blood cancers, gene therapies for neurological and ophthalmological diseases and engineered blood stem cell therapies for rare genetic diseases. These therapies have paved the way for massive academic and industry investment in the field. Today, it is estimated that there are over 2,600 industry and academic sponsored regenerative medicine trials ongoing worldwide[16]. At the same time, regulatory approvals remain uncommon in this evolving regulatory, manufacturing, and clinical landscape. CIRM will address this challenge and facilitate FDA approval of clinical programs.

Patient in **CIRM-Funded Clinical Trial** for Age-Related Macular Degeneration

Anna Kuehl was an avid nature lover but in her mid 30's, she was diagnosed with age-related macular degeneration (AMD), the leading cause of vision loss in the US. She gradually began losing the central vision in her left eye, could no longer make out people's faces clearly, drive a car, or read the time on her watch. Then she took part in a clinical trial funded by CIRM and conducted by Regenerative Patch Technologies. They implanted stem cells, seeded onto a scaffold, at the back of her eye. Kuehl says she noticed changes almost immediately. Anna's recovery suggests the need for continued research for the potential application of stem cell therapies for treatment of eye diseases.

Anna Kuehl


Evie Junior

Sickle Cell Disease Patient in a CIRM-Funded Clinical Trial

Evie Junior is a pioneer in the search for a cure for sickle cell disease, a painful, life-threatening condition. In July of 2020 he took part in a clinical trial where his own blood stem cells were genetically modified to correct the mutation that causes the disease. Those cells were returned to him and the hope is they'll create a sickle cell-free blood supply. Evie says he hasn't had any crippling bouts of pain or had to go to the hospital since his treatment. To demonstrate treatment efficacy, study investigators will continue to monitor the recovery of Evie and others in this clinical trial.

"Turning a promising drug candidate into an approved therapy requires overcoming many bottlenecks... CIRM's most effective and committed partner in accelerating this is the FDA."

— David W. Martin, MD, ICOC Board Member

5-Year Strategic Goals

Optimize CIRM's clinical trial funding partnership model to advance more therapies to FDA marketing approval

While the FDA's expedited designations support the growing regenerative medicine field, there is a need for streamlined and efficient approaches to enable more defined regulatory pathways to commercialization[17]. CIRM is uniquely positioned to develop these needed approaches.

CIRM's Clinical Program was purpose-built as a true partnership between CIRM and the awardee team where CIRM leverages internal and external expertise and resources to collaboratively achieve the project goals. CIRM's funding opportunities for translational and clinical stage programs align with FDA requirements and the funded activities are intended to provide the evidence base to support the development of these programs toward marketing approval.

Unique features of CIRM's partnership funding model include access to CIRM-funded strategic infrastructure such as the Alpha Stem Cell Clinics Network and the CIRM Cell and Gene Therapy Center as well as CIRM-sponsored advisory panels. As the field continues to mature and gain real world experience in navigating clinical development and regulatory approval for regenerative medicine therapies, CIRM's funding model will continue to evolve and adapt to the needs of its funded clinical trial projects. Areas of enhancement include advisory panels, funding for novel clinical trial designs and support for critical late-stage clinical and manufacturing development for regulatory approval.

CIRM's Clinical Advisory Panel (CAP) is an established system for CIRM and its external experts to work collaboratively with our programs to help them achieve their milestones, address bottlenecks, and prepare for the next stage of product development. The panels' recommendations have helped overcome manufacturing challenges, optimized clinical trial design, enhanced patient enrollment in trials and guided regulatory strategy. As more CIRM-funded clinical trials attain FDA-expedited designations and advance to later-stage clinical trials, it is imperative that CIRM provide these rapidly advancing projects access to regulatory guidance from experts who have driven projects to regulatory approval. We have the opportunity to develop a focused Marketing Approval Advisory Panel (MAAP) model, to build on this resource in crafting a regulatory approach to final FDA approval (BLA) while also considering for post-marketing plans and activities that would facilitate access and affordability (along with CIRM's Medical Affairs and Policy Team and as directed by CIRM's Accessibility and Affordability Working Group).

CIRM will also leverage the aforementioned research competency hubs (under Theme 1) to support the needs of its clinical programs and, in some cases, develop specialized clinical research competency hubs. As the field evolves, other potential enhancements to the Clinical Program could include supporting novel clinical trial designs such as adaptive trials or master protocol trials such as umbrella, platform and basket trials that efficiently test multiple hypotheses or therapeutic candidates.

5-Year Strategic Goals

Overcome manufacturing hurdles for the delivery of regenerative medicine therapies by building a public-private manufacturing partnership network

CIRM-Funded Academic GMP Facility Network

Industry Partners

- Manufacturing Services
- Resources
- Investment and Partnerships

INDUSTRY ALLIANCE PROGRAM

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

Another key impediment to regulatory approval of regenerative medicine products is manufacturing challenges because: 1) the products themselves are "living medicines" that have intrinsic variability in their quality attributes; 2) the manufacturing processes for these "living medicines" are complex and costly; and 3) arriving at quality attributes for novel products produced under novel manufacturing processes is challenging. Accordingly, "commercial ready" processes are typically delayed until later stages of clinical development, once the therapeutic candidate has demonstrated clinical proof of concept. While this is understandable from a financial and resource planning perspective, it has the net result of stacking a significant manufacturing bottleneck right before the regulatory approval finish line.

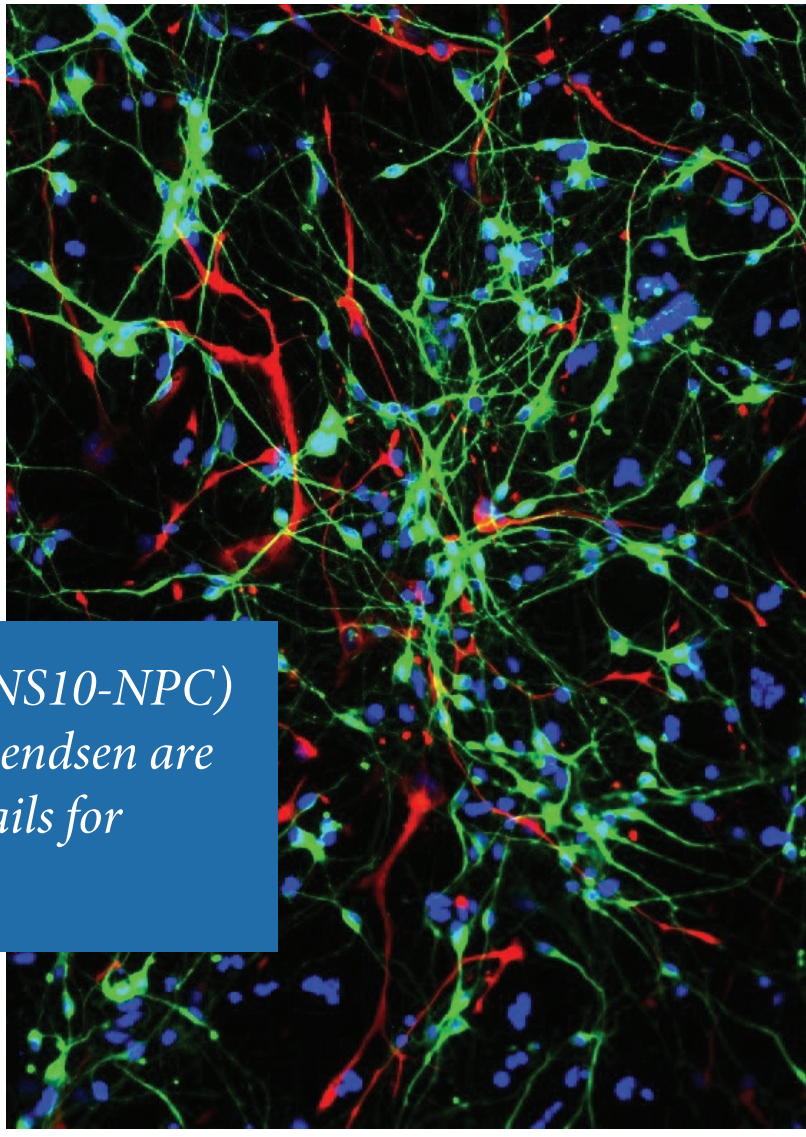
Compounding these barriers, there is also a talent pool gap and shortage in a trained manufacturing workforce for regenerative medicine products. California's current education and training infrastructure is unable to rapidly deploy expert personnel and leaders to keep up with the increasing workforce demand of the regenerative medicine manufacturing industry. There is a clear need for coordinated education and training programs in the state that not only meet the demand from the industry but also create efficient on-ramps for diverse workforce participation.

CIRM has defined the need for a California Manufacturing Network that combines academic innovation and industry expertise to address critical manufacturing and analytical bottlenecks and coordinates training programs that build a diverse and expertly trained manufacturing workforce in California.

CIRM will establish a statewide manufacturing network comprising academic process development and GMP manufacturing facilities and industry manufacturing partners to support the needs of a rapidly growing regenerative medicine industry in California, including workforce development. The network will de-risk the development of transformative regenerative medicine therapies, advance the development and adoption of manufacturing technology platforms, promote adoption of quality standards such as quality-by-design, and educate, train, and employ a diverse California workforce.

CIRM's California Manufacturing Network will require collaboration and coordination between academic institutions and industry manufacturing partners, including those within CIRM's Industry Alliance Program. CIRM will fund a network of academic GMP manufacturing facilities to enhance operations that will better support early process development, early GMP manufacturing and eventual transfer of the manufacturing process to industry partners. As a network, the academic GMP facilities would co-develop standardized approaches for technology transfer, and share specialized competencies and technologies. Industry partners, through their own business models, will provide access to early partnering opportunities for CIRM-funded projects, provide specialized materials and manufacturing technologies, analytics expertise, early and late-stage manufacturing capacity, and regulatory and quality expertise. In this way, member organizations would create synergies and produce output that would not be possible on their own.

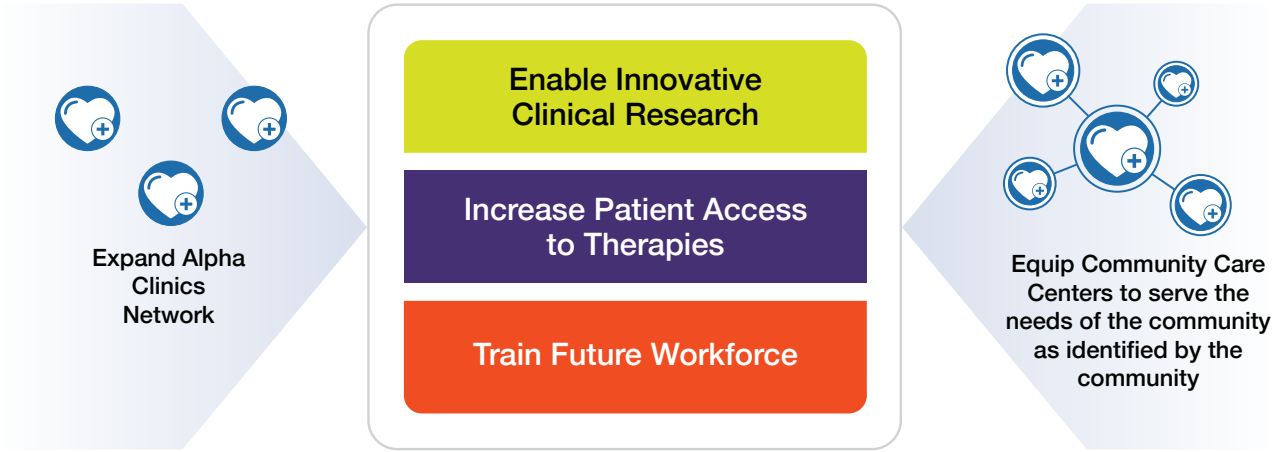
To address the need for a trained workforce in manufacturing, CIRM will leverage its existing education pillar programs and the California manufacturing network. CIRM, in collaboration with the California manufacturing network, will coordinate development of efficient and accessible education curricula and hands-on training programs for cell and gene therapy manufacturing at California community colleges and universities. CIRM will facilitate internship and certification programs across the California manufacturing network to support specialization and advancement opportunities in process development, manufacturing, and quality and CMC regulatory career pathways. Finally, it will help address the challenge of leadership turnover at California academic manufacturing facilities by supporting recruitment and mentoring programs for development of talented manufacturing leaders.



Human neural progenitor cells (CNS10-NPC) from the laboratory of Dr. Clive Svendsen are currently being tested in clinical trails for ALS and Retinitis Pigmentosa

5-Year Strategic Goals

Expand Alpha Clinics and create Community Care Centers of Excellence that support diverse patient participation in the rapidly maturing regenerative medicine landscape



When CIRM's Alpha Stem Cell Clinic Network was launched in the 2015, the prevailing need was to develop operational expertise for rapidly launching and executing patient-centered cell and gene therapy clinical trials at California's leading academic clinical research institutions[18]. The network was successfully expanded to 5 sites across 6 institutions and has supported the treatment of over 750 patients across 100 cell and gene trials from first-in-human academic trials to industry-sponsored post-marketing studies.

CIRM will expand the Alpha Clinics Network and will build a network of Community Care Centers of Excellence to ensure broad participation from California's diverse patient communities. While separate objectives with independent outcome measures, the expansion of Alpha Stem Cell Clinics and establishment of Community Care Centers are highly synergistic and will be addressed in tandem. The Alpha Stem Cell Clinics and Community Care Centers of Excellence will collaboratively achieve the goals of enabling innovative clinical research in regenerative medicine, increasing diverse patient access to transformative therapies, improving patient navigation of clinical trials[19], fostering collaborations between basic scientists and clinicians, educating the public and medical staff about emerging regenerative medicine approaches in the context of medical care and reinforcing the objectives of promoting equitable access to clinical trials and treatments to a diverse population. These clinical infrastructure progams will support the specialized training of a clinical research and healthcare workforce that is well trained to best serve patients who participate in regenerative medicine clinical trials or receive approved treatments. CIRM will support the Alpha Clinics Networks to establish competency hubs for technical expertise, facilities, and resources necessary to support novel clinical trial design.

It is well recognized that geographic disparities in clinical trial sites as well as and limited focus on community outreach and education about clinical trials have been shown to impede patient participation and contribute to the well-documented low participation[20] of under-represented patients in some studies[21,22]. Ultimately, lack of diversity in the clinical setting could significantly impact the success of trials, their likelihood for approval, and/or subsequent rate of long-term success. Thus, there is a need for expansion of clinical trial sites, and community involvement and outreach.

UC Davis Alpha Clinic

The Community Care Centers will serve the needs of patients in the community setting in 2 ways: 1) direct patient support through programs that will be designed to meet the unique needs of the given community; 2) leveraging the offerings of the Alpha Clinics Network where they could serve as referral and follow-up centers for the Network. By establishing the Community Care Centers of Excellence, CIRM will further expand and diversify patient participation in clinical research, which is heavily affected by structural (geographic availability), epistemological (patient education and outreach), and clinical design (eligibility, recruitment, and retention).

CIRM-funded Alpha Stem Cell Clinic Network and Community Care Centers will collaboratively extend geographic access to CIRM-supported clinical trials across the state. In coordination with or leveraging the Community Care Centers, patient advocacy groups and public health resources could expand improved outreach and navigation to patient communities best suited for CIRM-funded clinical trials. Community Care Centers have direct access to – and knowledge about – the needs of their patient populations including, culturally and linguistically effective community-based education and outreach. Thus, they are qualified and well-equipped to create a trusting environment where patients feel safe and supported in joining a clinical trial or utilizing an approved therapy. In parallel, Alpha Stem Cell Clinics would be designed to support the anticipated outreach and education efforts of future Community Care Centers. This synergistic approach between Alpha Stem Cell Clinics and Community Care Centers will "glue"[23] the stakeholders, significantly enhance diverse and equitable patient participation in clinical trial implementation[24], elevate the potential for regenerative medicine therapies to transform the well-being of the patients within the community, and ultimately increase the predictive probability of treatment success across many populations.

Both the expansion of Alpha Stem Cell Clinics Network and building of Community Care Center Network will also provide opportunities to train the future clinical research workforce. The training programs could range from supporting nursing development, specialty training for medical personnel, and training of clinical research personnel.

"To meet CIRM's mission of accelerating world class science to deliver real world solutions we are going to create Community Care Centers of Excellence in California. These centers will be critical in helping us engage diverse voices, identifying community concerns for underserved populations, and together, designing solutions to address cost and access to clinical trials and treatments for all Californians."

— Ysabel Duron, ICOC Board Member

Provide Opportunity for All

CIRM will build inclusive participation opportunities for all stakeholders, from the students to the workforce to the patients.

5-year Strategic Goals:

- **Build a diverse and highly skilled workforce** to support the growing regenerative medicine economy in California
- **Deliver a roadmap for access and affordability** of regenerative medicine for all California patients

As the field of regenerative medicine continues to grow, more treatment opportunities will present themselves to the community and eventually these will occur outside of the specialized academic centers. CIRM is committed to focused and deliberate actions to ensure that we serve a diverse patient community, and to provide access to clinical trials and to future approved treatments for these communities. While the aforementioned creation of healthcare infrastructure will further this goal, it will also require that we develop additional pathways to building strong communication channels, understanding, and a trusting relationship between the scientific community, healthcare providers and patients and general community. To accomplish this, we need to gain a better understanding of diverse views, cultures and perspectives of the various communities related to healthcare. We need to understand where regenerative medicine fits in their lives. We need to educate and develop a diverse workforce to be a part of this emerging field, and in bringing in this diverse perspective, we will enhance our understanding and this will help us to better serve the community. In addition, CIRM has been funded through Proposition 14, to develop approaches to increase access and affordability to the transformative treatments that it funds and the aforementioned considerations are critical to these efforts as well.

Build a Diverse and Highly Skilled Workforce

The rapidly advancing regenerative medicine field provides myriad opportunities for broad participation in its growth but the increasing scale and sophistication also raises the risk of it leaving many stakeholder groups behind. As the regenerative medicine field matures, it is incumbent upon us to train the next generation of researchers, leaders and innovators. There is a growing demand for education and experience requirements while a dearth of reliable pathways to gain practical, hands-on experience. CIRM is uniquely positioned to address this need.

CIRM, in its continued commitment to building education and training programs, will have the opportunity to build a diverse, highly skilled regenerative medicine workforce. CIRM has created "on-ramps" to pursue further training or careers in the regenerative medicine field. There is an opportunity to create additional on-ramps, providing access for those from other fields of specialty, to rapidly advance in regenerative medicine career pathways such as manufacturing, clinical research, treatment delivery or patient navigation[25].

Deliver a Roadmap for Accesibility and Affordability

Additionally, as Proposition 14 stipulates, an Accessibility and Affordability Working Group (AAWG) will be formed to take deliberate action on increasing diverse patient access to both investigational and approved regenerative medicine therapies. The AAWG will set priorities and a direction, in coordination with the CIRM team to provide opportunities for patients to gain support in their participation in regenerative medicine clinical trials and in accessing approved treatments that were developed through CIRM funding.

"Stigma remains a significant barrier that impacts the ability to provide care – particularly among racially and ethnically diverse communities. In my own practice, I've seen how stigma can prevent individuals from entering into care even when access issues have been mitigated. Public awareness campaigns, and culturally specific advocacy efforts and practices must be integrated into treatment models in order to provide individuals with the specific care they need. CIRM is uniquely positioned to assist in these efforts as it works to enact its commitment to diversify the types of projects it funds by engaging in targeted outreach to diverse sectors and communities."

— Le Ondra Clark Harvey, PhD, ICOC Board Member

Alessandra Rodriguez y Baena,

CIRM Bridges Scholar and PhD Candidate at UC Santa Cruz

Alessandra was a Master's student at Cal Poly, San Luis Obispo. With the support of CIRM's BRIDGES program, she became a CIRM intern in the Willert Lab at UC San Diego. Alessandra is now a fourth-year PhD student at the Forsberg Lab in the department of Molecular, Cell & Developmental Biology at UC Santa Cruz where she is studying the epigenetic regulation of aging in bone marrow stem cells. Alessandra captures CIRM's commitment to educating the future workforce of regenerative medicine in California.

"The CIRM Bridges program at Cal Poly provided me with supportive mentors (both at Cal Poly and UCSD), hands-on training in the exciting field of regenerative medicine, and incredible exposure to innovative ideas and research. I always recommend my undergraduate students who are interested in research to apply to the Bridges programs because, to me, it was a defining experience that led me to pursue my passion for stem cell research as well as teaching."

— Alessandra Rodriguez y Baena, CIRM Bridges Scholar Alumnus

5-Year Strategic Goals

Build a diverse and highly skilled workforce to support the growing regenerative medicine economy in California

Training and educating individuals with wide swaths of backgrounds, perspectives, and skills enhances development of the entire cell and gene therapy discovery and delivery pipeline, from basic and clinical research to manufacturing and commercialization.

Through its existing Educational (EDUC) pillar programs such as SPARK and Bridges, CIRM has already demonstrated its commitment to supporting a diverse and inclusive next generation of stem cell scientists. These programs offered unique training and career development opportunities to underrepresented students and have facilitated their professional readiness for successful stem cell careers.

CIRM will augment training and education of the future California workforce by building on-ramps that facilitate rapid career entry, accelerate career advancement, and provide greater access for diverse and underrepresented groups. Effective use of on-ramps will require coordination between academia and industry on development of education curricula, degree or certificate requirements, hands-on training programs, and career advancement pathways. For example, CIRM will connect its existing EDUC pillar programs with the planned California Manufacturing Network infrastructure program to address the critical need for a highly trained manufacturing workforce in the rapidly growing cell and gene therapy industry of California. It will foster collaboration between community colleges, universities, academic and process development/manufacturing facilities, and the biotech companies to develop efficient education, hands-on training, and on-the-ground experience-building programs for entry or advancement in process development, manufacturing, and quality career pathways. It will similarly leverage Alpha Clinics and Community Care Centers to develop education curricula to address the currently unmet need of generating diverse, trained, and culturally aware Clinical Research Coordinators (CRCs), to enhance patient experience and access to clinical research. In short, the workforce training programs can be combined with CIRM's other pillar programs to build on-ramps for career pathways across many areas such as basic, translational and clinical research, clinical trial operations, regulatory sciences, data science, healthcare delivery, science communication, patient navigation, and community engagement.

Additionally, CIRM-funded education programs will have built-in accountability for developing more robust models to promote representation of our diverse community and inclusion of underserved and under-represented communities. These programs will be funded to develop innovative approaches to accomplish their objectives. The CIRM model lends itself to the coordination of these efforts across host institutions in California that will train thousands of students in the upcoming years.

Success Stories: Education and Training Grants

Under Proposition 71, Derrick Rossi was one of the first scholars to receive CIRM funding through the Stanford Comprehensive Training Grant, which was offered at 3 levels of pre- and post-doctoral and clinical. After completing his post-doctoral training at Stanford, Dr. Rossi set out to use synthetic modified messenger RNA (mRNA) for safe and efficient iPSC reprogramming as a new faculty member at Harvard University. His discovery later catapulted the launch of Moderna, which sought to apply the mRNA technology platform to cancer vaccines and eventually pivoted to infectious diseases. In 2020 and in the wake of a pandemic, Moderna collaborated with the NIH in rapidly applying its mRNA technology platform to develop what became one of the main sources of the COVID-19 vaccine for billions of people world-wide. Dr. Rossi is just one, albeit now well-recognized, success story from CIRM's education and training grants. In its current strategic plan, CIRM seeks to augment this program by providing a diverse array of on-ramps that will facilitate training of the future CA workforce across many career paths.

"As we are witnessing across the U.S. economy, challenges in recruitment to fill open research staff positions, and retention of research staff is now a major crisis. To advance the mission of CIRM... we need to create new opportunities for individuals to recognize biomedical research as a career opportunity."

— Pat Levitt, PhD, ICOC Board Member

5-Year Strategic Goals

Deliver a roadmap for access and affordability of regenerative medicine for all California patients

As CIRM is driving more transformative regenerative medicine therapies to the clinics, we will need to address the challenge of accessibility and affordability of these treatments to all patient communities in the real world.

Traditional reimbursement models by private insurers or government payers, typically pay for each treatment or interaction with the healthcare system over the course of years, and often throughout a patient's life for chronic disease. The regenerative medicine treatments (cell and gene therapies) that are being supported by CIRM are designed to durably address the unmet medical need, in many cases require a single or limited treatment, and, in some cases, are curative. While these regenerative medicine treatments can result in significant long-term savings, they have high upfront costs, which are generally incompatible with current reimbursement models.

The CIRM team, in coordination with the newly created Accessibility and Affordability Working Group, will develop a Roadmap to overcome these hurdles. This roadmap will include a strategy for gathering the necessary data and information to support reimbursement for regenerative medicine products that result from CIRM's programs, a plan to engage with policymakers and regulators, and the development of novel healthcare delivery models that can be implemented and refined within the Alpha Clinics Network and future Community Care Centers of Excellence.

"Our new working group will reach out to potential clinical trial patients and their caregivers to be part of an infrastructure which provides accessible and affordable new treatments."

— Senator Art Torres, JD, Vice Chair of the ICOC

Real Life™

Strategic Plan Summary

CIRM's proposed 5-year strategic goals
in each of the three thematic areas are summarized below.

Advance

World Class Science

- Develop next-generation **technology competency hubs** that broadly empower and connect California's research ecosystem
- Build **knowledge networks** that foster and advance novel discovery, translational and clinical research approaches

Deliver

Real World Solutions

- **Optimize CIRM's clinical trial funding partnership** model to advance more therapies to FDA marketing approval
- **Overcome manufacturing hurdles** for the delivery of regenerative medicine therapies by building a public-private manufacturing partnership network
- **Expand Alpha Clinics and create Community Care Centers of Excellence** that support diverse patient participation in the rapidly maturing regenerative medicine landscape

Provide

Opportunity for All

- **Build a diverse and highly skilled workforce** to support the growing regenerative medicine economy in California
- **Deliver a roadmap for access and affordability** of regenerative medicine for all California patients

CIRM will achieve the 5-year goals for each of the three strategic themes by enhancing, organizing, and interconnecting its proven funding model.

Under the direction of the President & CEO, the CIRM teams execute all functions of the agency from launching new grant funding opportunities, to managing active awards, to outreach, engagement, and partnerships with external stakeholders.

SCIENTIFIC PROGRAMS

The Scientific Programs Team identifies, promotes, and sustains new stem cell and gene therapy technologies with the greatest potential to improve patient care and drives their progression toward clinical use. The team also supports programs that build the next-generation workforce in California to tackle the current and future challenges of delivering cutting edge treatments to all members or our community. As part of this strategic plan, the team will foster a collaborative ecosystem to enable large scale data analyses for collaborative discoveries.

THERAPEUTIC DEVELOPMENT

The Therapeutics Development team identifies and recruits innovative development stage cell and gene therapy projects eligible for CIRM funding and manages these projects for success once funded. The team is composed of senior scientists with expertise in multiple therapeutic areas including manufacturing, preclinical and clinical development, regulatory affairs, and project management.

REVIEW

The Review Team maintains a rigorous and efficient review process that helps CIRM achieve its strategic goals and focuses efforts on three key elements. The first is to cultivate a world class team of expert reviewers that embrace the CIRM mission and seek to improve review performance. Second is to direct a rigorous review process that adheres to all applicable rules and selects for the most highly meritorious projects. Finally, the team aims to rapidly and objectively communicate program rules, procedures, and outcomes to all stakeholders including CIRM's Governing Board, which makes the final decisions on funding.

OPERATIONS

The Operations team is a cross-functional team that partners across the organization to create critical infrastructure and operational support by fostering growth and talent, implementing new systems and tools, establishing effective policies, monitoring compliance, and reporting portfolio performance.

FINANCE

The Finance Team is responsible for the financial control systems of Prop 71 and Prop 14 bond proceeds including short-term and long-term portfolio modeling, cashflow management, resource allocation strategy, and annual fiscal reporting to the Citizens Financial Accountability Oversight Committee. It also supports the CIRM team by providing budgeting, accounting, facility management, asset management, mail delivery, and document management services. In providing procurement services, the Fiscal Services acknowledges the role of diversity and inclusion in the procurement and contracting of goods and services for CIRM and how it can support financial performance and overall effectiveness of the organization.

PUBLIC OUTREACH AND BOARD GOVERNANCE

The Public Outreach and Board Governance team is responsible for communicating CIRM's mission to the diverse California public through the CIRM website, blog and social media channels, as well as in-person events. This team works directly with CIRM's Governing Board to advance CIRM's mission and to lead the development and coordination of Board policies and procedures. It also works with California state legislators and staff members as well as patient advocates to keep them up-to-date on the full scope of CIRM's activities.

BUSINESS DEVELOPMENT

The Business Development team collaborates with external stakeholders to advance CIRM's mission. The team manages the Industry Alliance Program, which facilitates industry partnerships with CIRM's portfolio projects to accelerate commercialization of CIRM-funded therapies. It also supports CIRM's alliances with industry partners, funding agencies and other stakeholders to meet the resource, partnering and strategic needs of CIRM's funding programs. Under this strategic plan, the team will drive development and coordination of the California Manufacturing Network.

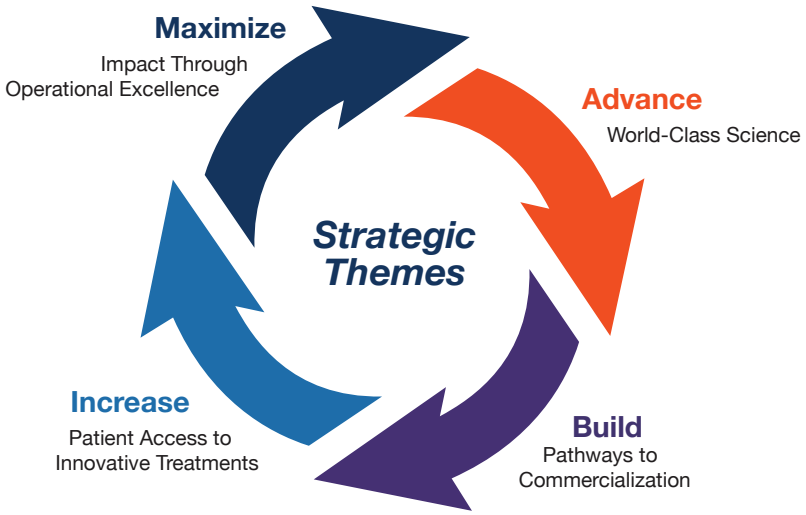
MEDICAL AFFAIRS AND POLICY

The Medical Affairs and Policy Team will support the development of CIRM's Roadmap for Affordability and Accessibility in coordination with CIRM's Working Group. It will also manage future initiatives involving post-market research, follow-up and outcome database, registry development, real world evidence research, healthcare economics analysis, and patient-reported outcomes. This group will manage the Alpha Stem Cell Clinics Network expansion and the future Community Care Centers of Excellence, both of which are designed to deliver equitable access to clinical trials and approved treatments arising from CIRM's programs. The Medical Affairs and Policy group will work in coordination with the CIRM core programs to drive the goals of CIRM's accessibility and affordability roadmap.

Strategic Planning Process

This strategic plan was conceived and organized using the following methodology. CIRM was internally organized into four project teams spanning four thematic areas: advance world class science, build pathways to commercialization, increase patient access to innovative treatments and maximize impact through operational excellence. The four project teams sought expert stakeholder input, assessed CIRM funding program outcomes, performed needs assessments and reviewed Proposition 14 stipulations to develop initial strategic concepts for their respective thematic areas. The aggregate output from the 4 project teams was continually refined with input from stakeholders to develop the final strategic plan.

Internal CIRM Project Teams



Continual input from CIRM stakeholders and external key opinion leaders (KOLs) was critical to the development of the strategic plan. Key stakeholder groups included the ICOC, Grants Working Group, patient community, CIRM's scientific and clinical research communities, CA educational institutions, CIRM-funded companies and industry alliance program members.

CIRM program meetings and workshops afforded the opportunity for multi-stakeholder input on broad topics. In addition, CIRM hosted focused speaker panels, meetings, and workshops to gain deeper insight and feedback on specific topics. For example, the 2020 Alpha Clinics Symposium not only provided stakeholder input on the value of the Alpha Stem Cell Clinics Network but the CIRM-hosted Patient Access & DEI Panel brought together insights from CIRM ICOC patient advocates, patient representatives and external KOLs on promoting diversity, equity and inclusion in clinical research. Similarly, the Strategic Scientific Advisory Panel Meeting[26] brought together ICOC members, CIRM researchers, external KOLs representing academia, FDA, NIH, and industry to discuss high-impact focus areas for CIRM funding, particularly in neuroscience. The Manufacturing in California Workshop was focused on promoting discussion between ICOC members and manufacturing leaders of California academic GMP facilities, CIRM grantees, industry alliance program members, and the manufacturing industry on the prospect of building a statewide manufacturing network for cell and gene therapies.

Broad Stakeholder Input

- 2020-2021 ICOC Meetings
- Stakeholder Town Hall Meeting and Survey
- Strategic Scientific Advisory Panel Meeting
- Brainstorming Neurodegeneration Workshop
- GWG Program Meeting
- CIRM Program Meetings
  - Grantee Meeting
  - Alpha Clinics Symposium
  - Bridges & SPARK meetings

Patient & Community

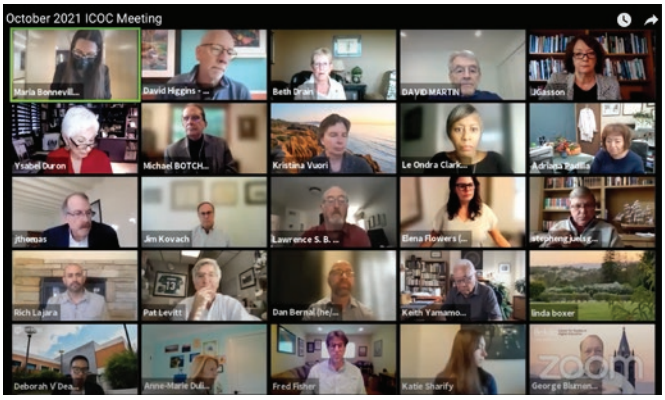
- Patient Navigation Roundtable
- Alpha Clinics Symposium: Patient Access & DEI Panel

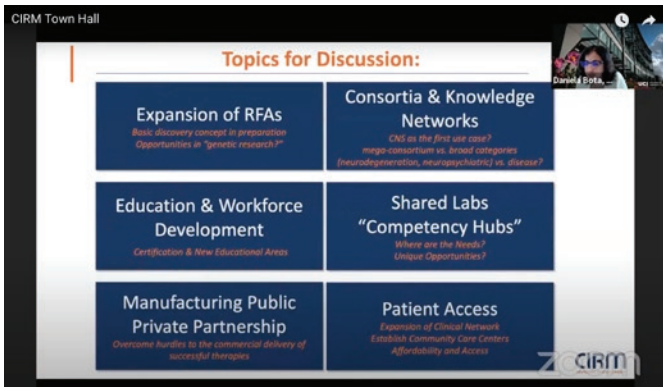
Knowledge Networks

- Grantee Meeting: Knowledge Networks Panel
- Data Biosphere Planning Committee Meeting
- Shared Labs Survey

Manufacturing & Commercialization

- Industry Alliance Program Meeting
- Industry Partner Day
- Manufacturing in California Workshop
- GMP Manufacturing Facility Survey





Patient & Community

- Patient Navigation Roundtable
- Alpha Clinics Symposium: Patient Access & DEI Panel

Knowledge Networks

- Grantee Meeting: Knowledge Networks Panel
- Data Biosphere Planning Committee Meeting
- Shared Labs Survey

Manufacturing & Commercialization

- Industry Alliance Program Meeting
- Industry Partner Day
- Manufacturing in California Workshop
- GMP Manufacturing Facility Survey

Endnotes

[1] For further reading, please see: Sambrano, G. and Millan, M. Translating Science into the Clinic: The Role of Funding Agencies. Cell Stem Cell, 2020.

[2] Wei and Rose. Economic Impacts of the California Institute for Regenerative Medicine (CIRM). USC 2019.

[3] Patel, S., Talib, S. and Millan, M. Boldly De-Risking Development of Impactful Cell and Gene Therapies: The California Stem Cell Agency's $3B Funding Model. Cell & Gene Therapy Insights, 2020.

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[5] 2019-20 CIRM Annual Report

[6] Dobrindt et al. Publicly Available hiPSC Lines with Extreme Polygenic Risk Scores for Modeling Schizophrenia. Complex Psych. 2020.

[7] CIRM Strategic Scientific Advisory Panel Meeting Summary, Feb 2021

[8] CIRM Brainstorming Neurodegeneration Workshop Summary, Apr 2019

[9] Meder et al. Institutional core facilities: prerequisite for breakthroughs in the life sciences. EMBO Rep. 2016.

[10] Rick Horwitz, Ekemini A.U. Riley, Maria T. Millan, et al. It's time to incorporate diversity into our basic science and disease models. In press.

[11] In line with survey results obtained from CA research and teaching institutions. Please see CIRM Town Hall 2021 Survey Results Topline.

[12] CNS Consortium 2022 Workshop Planning Committee Meeting Executive Summary, Sep 2021

[13] CIRM Brainstorming Neurodegeneration Workshop Summary, Apr 2019

[14] In line with survey results obtained from CA research institutions. Please see CIRM Town Hall 2021 Survey Results Topline.

[15] Approved cell and gene therapy products

[16] Alliance for Regenerative Medicine 1H2021 Report

[17] In line with survey results obtained from CA research institutions. Please see CIRM Town Hall 2021 Survey Results Topline.

[18] Jamieson, C., Millan, M. et al. CIRM Alpha Stem Cell Clinics: Collaboratively Addressing Regenerative Medicine Challenges. Cell Stem Cell, 2018.

[19] CIRM Patient Navigation Roundtable Summary, Jan 2020

[20] Feyman et al. Disparities in clinical trial access across US urban areas. JAMA Netw Open. 2020.

[21] https://www.nap.edu/read/24624/chapter/1#iii

[22] Chen C, Wong R. Black patients miss out on promising cancer drugs. ProPublica. 2018.

[23] National Academies of Sciences, Engineering, and Medicine. 2017. Communities in Action: Pathways to Health Equity. Washington, DC: The National Academies Press. Chapter 4.

[24] PhRMA Press Release. Five Key Strategies for Enhancing Diversity in Clinical Trials. Nov 2021.

[25] In line with survey results obtained from CA research and teaching institutions, as well as past and potential future trainees. Please see CIRM Town Hall 2021 Survey Results Topline.

[26] CIRM Strategic Scientific Advisory Panel Meeting Summary, Feb 2021

World Class Science | Real World Solutions

Opportunity for All