CURE

Beyond CIRM 2.0

CALIFORNIA'S STEM CELL AGENCY

now it's personal

Proposed Strategic Plan

2016 & Beyond

HOPE

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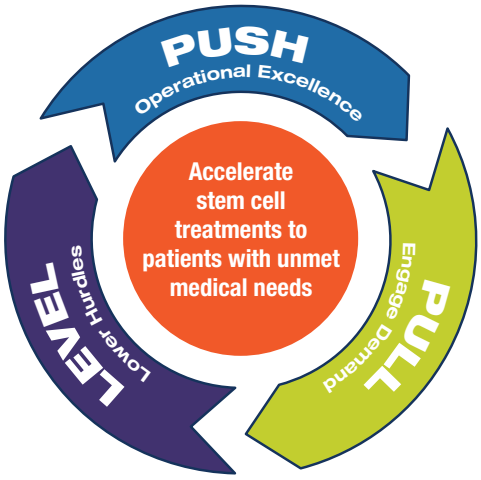


MISSION | To accelerate stem cell treatments to patients with unmet medical needs.

Beyond CIRM 2.0

1 Introduction

A bold vision for maximizing CIRM's impact... for those who need it most.

MISSION | To accelerate stem cell treatments to patients with unmet medical needs.

Beyond CIRM 2.0

1 Introduction

CIRM has undertaken this strategic planning process in an effort to optimize its performance over the next five-year period (2016-2020). This period was selected because it is the timeframe for which the Institute is certain to have funds available to make additional investments.

This process, along with the final strategic plan, will provide several key benefits to CIRM stakeholders, outlined below:

Situational Awareness

The planning process is a unique opportunity to evaluate changes and challenges in our environment since the last strategic plan was enacted in 2012 and consider implementation of new ideas or changes in course.

Organizational Clarity

After this process, our mission will be clear, and those responsible for fulfilling it will embrace it with conviction. A clear mission leads to clear priorities and direction. These priorities will align our efforts, increasing our output and results.

Measurable Goals

For goals to be effective, we must be able to measure our progress against them without debate or room for interpretation. With measurable goals, if we are not on track, we will be able to adjust our course in time to allow us to meet our targets. We are setting concrete, tangible goals through this process.

The format of this document is intended to take the reader from an understanding of where CIRM came from and stands now, through to a plan that ensures maximum success for the Institute moving forward. It starts with overarching, guiding concepts and moves to specific actions and outcomes, building progressively and adding more detail in each section.

Throughout the strategic planning effort, CIRM was committed to a process, no matter how difficult, that would produce a roadmap that provides the greatest likelihood of CIRM achieving its mission.

A key theme of this strategic planning process was not to settle for "good enough." Nor could we simply organize the items on various key stakeholders' wish lists to follow the path of least resistance. We did not intend to create a product that made bold or flashy statements predicting a grand new path for the Institute, nor did we intend to simply validate the current course. Instead, the purpose was to do what was right and necessary, whatever that may be, to best accomplish the mission and help the people we serve.

The team worked like people's lives depended upon the outcome of the planning effort and subsequent implementation… because they do.

2 About CIRM

CIRM's mission, under the authority of Proposition 71, is to accelerate stem cell treatments to patients with unmet medical needs.

MISSION | To accelerate stem cell treatments to patients with unmet medical needs.

2 About CIRM

Proposition 71 arose from the people of California's desire to realize the promise of stem cell treatments to provide relief to patients with serious unmet medical needs and their frustration with limitations on federal funding for human embryonic stem cell research. Accordingly, patient advocates and researchers joined forces to create a vehicle to fund stem cell research in California. On November 2, 2004, 59% of the voters approved Proposition 71, which amended the California Constitution to establish the right to conduct stem cell research in California and authorize $3 billion to fund stem cell research.

Specific Aims and Scope of Proposition

In authorizing these funds, Californians expected to speed the delivery of stem cell treatments and cures to patients with unmet medical needs, including a priority for funding pluripotent and progenitor cell research that was not receiving timely or sufficient federal funding. Additional potential benefits to Californians include propelling California into a leadership position in regenerative medicine, establishing California as the premier international location to advance stem cell medicine, stimulating the economy, reducing health care costs by replacing chronic treatments with cures, and ensuring that the State has the opportunity to benefit from the potential receipt of royalty payments arising from CIRM-funded treatments or technologies.

About the Governing Board

CIRM is governed by a 29-member Governing Board, the Independent Citizens' Oversight Committee (ICOC), which is composed of leaders in California from the patient advocate, biotechnology industry, and biomedical research sectors. In addition to its fiduciary responsibility to the people of California, the Board is charged with: (1) adopting scientific, medical, ethical, and intellectual property policies; (2) making final funding decisions on grant and loan awards; and (3) providing oversight of CIRM.

2 About CIRM

CIRM's Board is composed of three groups, consisting of patient advocates, biotechnology industry leaders, and science and academic leaders. These groups have sufficiently broad expertise to ensure that the Institute's focus is on the people who need cures for serious disease and injury; to push the Institute to accelerate the involvement of industry in the delivery of stem cell treatments and cures to patients and leverage industry resources to achieve CIRM's mission; and to provide the Institute with the scientific expertise and research management experience needed for oversight of the Institute's funding decisions and operations.

The California Institute for Regenerative Medicine

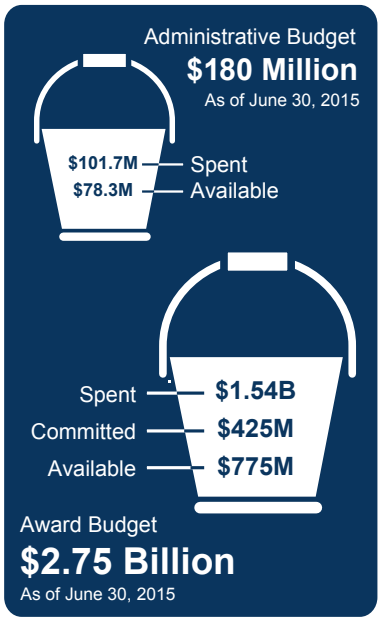
The Institute was established by the passage of Proposition 71 and held the first CIRM Board meeting on December 17, 2004, to begin the complex task of building a research funding institute from scratch. While overcoming two constitutional challenges to Proposition 71, CIRM relied on a loan of $150 million approved by then Governor Schwarzenegger and $35 million in contingent bond anticipation notes, to hire a skeleton staff to establish the Institute. Initial activities included:

- establishing governance policies and structures;
- determining funding priorities;
- creating an application and review process;
- developing systems to manage review, award, and finance processes; and
- creating an administration process to manage approved awards.

The Institute made its first awards in 2006 using the contingency funds, and the first stem cell research bonds were issued to CIRM in 2007 after the California Supreme Court declined to review the appeal of the unanimous decision of the Court of Appeal upholding the constitutionality of Proposition 71.

MISSION | To accelerate stem cell treatments to patients with unmet medical needs.

2 About CIRM



CIRM Funding (as of FY Ending 2014/2015)

Proposition 71 allocated a total of $3 billion in general obligation bonds to CIRM. CIRM funds are separated into two distinct categories, Administrative and Research. A total of $180M, or 6% of the total amount authorized by the bond act, is available for administrative costs for the lifetime of the Institute. After covering capitalized interest costs of the bonds for the first five years and the ongoing costs associated with the bond issuance, a total of $2.75B was made available for research grant and loan awards.

CIRM Program Areas

From 2006 through 2014, CIRM executed on its mission through initiative-based funding where CIRM issued individual funding announcements describing a specific and singular scope of research and requesting the submission of applications responsive to those needs during a specified one-time submission window. While this resulted in the funding of projects that advanced the field of stem cell research and in the initiation of approximately 10 clinical trials, each initiative was focused only on achieving its own objective and was not necessarily integrated with other initiatives to advance CIRM's mission.

In 2015, with the launch of the CIRM 2.0 Clinical Program, CIRM shifted to a systems-based approach to partnering with researchers to advance its mission.

Using this approach to funding, CIRM is focused on coordinating all its efforts to overcome obstacles to the achievement of the CIRM mission to accelerate stem cell treatments to patients with unmet medical needs.

MISSION | To accelerate stem cell treatments to patients with unmet medical needs.

2 About CIRM

CIRM invests in 5 Program areas:

INFRASTRUCTURE

The CIRM Infrastructure Program builds real and virtual centers that provide the resources, expertise, and information necessary to more efficiently advance CIRM's programs and projects.

EDUCATION

CIRM's Education Programs support the development of a workforce qualified to drive achievement of the CIRM mission, now and in the future.

DISCOVERY

The Discovery Program supports the exploration of new, potentially groundbreaking stem cell based treatments and technologies from their inception to translation.

TRANSLATION

The Translation Program supports the acceleration of early development activities necessary to prepare stem cell treatments, devices, or tools for clinical study.

CLINICAL

The Clinical Program supports the acceleration of high-quality clinical trials of stem cell treatments to address unmet medical needs.

3 CIRM Today

It's a new day. The CIRM 2.0 Clinical Program reduces time for awards from 22 months to approximately 120 days.

MISSION | To accelerate stem cell treatments to patients with unmet medical needs.

3 CIRM Today

Throughout our entire strategic planning process, we conducted robust and inclusive field outreach to our stakeholders. We held one-on-one meetings, visited academic centers, sought out and received input from Board members, and listened to many patients and patient advocates. This information gathering process provided us with a broader and more comprehensive perspective. We then spent time absorbing, distilling, and synthesizing the information and what it meant for CIRM's future.

Five key themes emerged from this process, and these themes shaped and influenced every part of the resulting strategic plan. These are described in the sections below.

Initiative-based approach

It is easy to forget that in the early days of CIRM the field of stem stem cell treatments looked very different than it does today.While numerous diseases were being studied, the volume of research within each disease area was much smaller than it is today, especially in translational, and clinical research. There simply was not adequate activity, nor resources within CIRM, to sustain programs designed to carry development of stem cell treatments forward from a beginning to an ending point. Thus at the time CIRM was designed to accommodate a lower volume of applications, leading to CIRM's adoption of an initiative-based approach, where we waited for critical mass to build in an area, released a request for applications (RFA), and issued awards in response to the RFA. This represented a necessarily opportunistic approach to research; however, it was not predictable nor was it synchronous.

At a micro level, this approach was highly responsive to the needs of the time but at a macro level it created uncertainty among the research community regarding the possibility and timing of future research prospects.

Now that there is critical mass in the field, it is time to improve our process. A systems-based approach allows us to create a continuum of research and development opportunities, with predictable and timely offerings, resulting in a more efficient process overall. We have already seen early benefits of this systems-based approach with the introduction of the CIRM 2.0 Clinical Program. During its first nine months, 25 applications were received and processed by CIRM (up from four in all of 2014) with the average time from application to award dropping from 22 months, under the previous system, to less than four months today.

Translation – Still "The Valley of Death"

Another theme was the level of difficulty and length of time needed to move a newly discovered stem cell treatment candidate through preclinical development into clinical trials. Clinical development can begin once an IND, or Investigational New Drug application, is cleared by the Food and Drug Administration (FDA). This allows a potential treatment to be administered to patients in clinical trials as required to ultimately obtain regulatory approval. Due to the high failure rate, this stage of development has been termed "the valley of death."

For stem cell treatments, the average length of time to conduct the research and IND-enabling preclinical studies necessary to obtain an IND is approximately 8 years, compared to 3.2 years for traditional pharma and biotech drugs.

The reason for this is multi-factorial. First, the FDA has applied the drug development model for a conventional drug to stem cell treatments, which is like forcing a round peg into a square hole. Next, the scope of studies required is large, and optimal study designs are not well understood or well-defined by regulatory agencies. Secondly, funding agencies, such as NIH and CIRM, have not always provided a continuous path of funding opportunities which can significantly slow the pace of development. Lastly, a lack of familiarity among investigators with the requirements for IND approval further lengthens the time to a successful filing. These clearly are opportunities for CIRM to leverage its resources and improve the odds for success.

3 CIRM Today

Minimal Industry Involvement

Currently CIRM funds predominantly go to academic researchers and institutions, with a disproportionately small share awarded to industry. In fact, 91% of all CIRM dollars to date have been disbursed to academic institutions. Insufficient industry involvement is also reflected in the track record of tech transfer offices at academic institutions. Out of 3,400 technologies currently marketed by the UC System, less than 2% are stem cell programs and only 8% of CIRM's therapeutic programs are partnered.

Research efforts in academic institutions are essential to the development of groundbreaking therapies, but without industry involvement, there is no path forward through to the types of clinical trials and related efforts which are necessary to get treatments approved by regulatory agencies so that they can become available to all patients.

Regulatory Challenges

CIRM's stakeholders emphatically voiced concerns over the enormous regulatory challenges facing stem cell treatments. In fact, 70% of respondents to our survey listed the FDA as the biggest impediment for the development of stem cell treatments. To many the regulatory requirements imposed by the FDA appear to be increasing despite an ever growing body of work demonstrating safety. As a result, companies, and sadly patients, must often go outside the United States to be able to conduct trials and gain access to treatments. As one stakeholder said:

> *"Is perfect becoming the enemy of better? One recent treatment touted by the FDA as a regulatory success had such a high clinical development hurdle placed on it that by the time it was finally approved, standard of care had evolved. When it was finally approved, five years later, its market potential had significantly eroded and the product failed commercially."*

The regulatory framework for the development of human cells and tissues into therapies for patients has been in place in the US for 15 years, without a single stem cell product being approved. Japan, recognizing that a different regulatory approach was needed to combat this stagnation took action and in 2014 enacted the Regenerative Medicine Promotion Act which created an expedited pathway for regenerative therapies in Japan. Japan subsequently approved their first stem cell treatment in September of 2015.

Thus far the FDA does not appear to have the same commitment and motivation as Japanese regulators. In fact the FDA recently began providing members of the U.S. Congress with one-side information, reporting only the dangers of stem cell treatments, much of which was outdated. In these representations, the FDA failed to provided a balanced picture of the safety record of stem cell treatments, which is actually well documented in the clinical literature. These actions cast the FDA in a very unfavorable light and make it appear they are not just not helping, but are actively lobbying against a therapeutic modality for which they are responsible for fostering.

CIRM needs to join with Congress, academia and industry, and patients, to bring about real change to appropriately level the playing field for testing and approval of these promising therapies via FDA regulations.

Patient Advocacy Participation

The final theme of the strategic plan is an appeal for increased participation by patient advocates. This is a powerful group of highly motivated individuals because they live with, and battle every day, the very diseases that CIRM investigators study. They want to play a larger role and contribute to CIRM's activities and success. Their input strongly influenced the design of this strategic plan.

4 Mission Confirmation

Let's Go!

4 Mission Confirmation

An essential step in the development of a strategic plan is clearly defining a mission for the organization. In the case of an existing entity such as CIRM, the task involves either confirming or modifying the previously established mission.

To accomplish this, CIRM conducted surveys of both its Board members and external stakeholders.

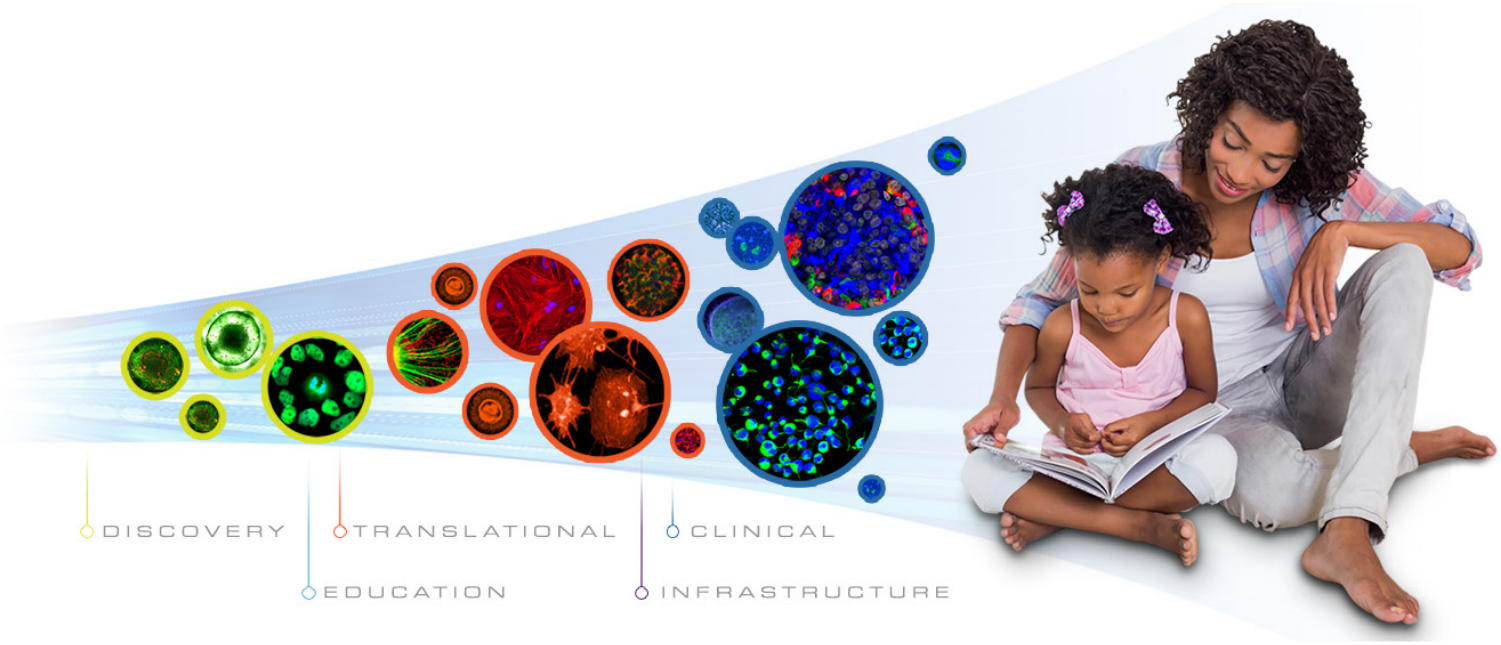
The survey asked respondents:

Do you agree that the mission of CIRM should be "to accelerate stem cell treatments for patients with unmet medical needs?"

The results were unequivocal. One hundred percent (100%) of Board members agreed with this statement. Results of the survey of external stakeholders were similar, with 95.4% of respondents (207 of 215) agreeing that CIRM's mission should be to accelerate stem cell treatments to patients with unmet medical needs.

5 Overarching Vision

Exponentially advance CIRM's mission



5 Overarching Vision

With the mission well established, we move to the next level of detail on the plan – Vision. Specifically, what we want CIRM to look like over the next five years.

The overarching five-year vision embodied in this plan is to:

> *Exponentially advance CIRM's mission by leading a coordinated campaign that holistically attacks the obstacles meaningfully affecting the speed, probability and sustainability of stem cell treatments to help patients in need.*

We choose these words with intent.

"Exponentially advance…"

This phrase conveys the magnitude of the impact CIRM intends to make over the next five years. Building upon the previous efforts of the organization, the expectation is that the rate of progress will increase and CIRM will make objective and measureable progress at an accelerated pace when compared to the Institute's earlier efforts.

"…CIRM's mission…"

Mission drift can reduce productivity by diluting an organization's efforts with non-mission critical activities. The often redundant use of and reference to the CIRM mission within this statement and throughout this document is intentional and meant to reinforce alignment amongst CIRM's various stakeholders and prevent mission drift.

"…by leading…"

Many stakeholders requested more leadership from CIRM. The cost of leadership is usually minor compared to its beneficial effects, making it not only an effective, but efficient strategic element.

5 Overarching Vision

"...a coordinated campaign..."

Historically, CIRM has employed an initiative-based strategy in which programs were run essentially independently of one another. Under this plan, there will be a complete transition from an initiative-based approach into a systems-based approach, wherein every program will be integrated into and coordinated with the overall effort to accomplish the mission. As with leadership, coordination produces synergies with negligible added cost.

"...that holistically attacks the obstacles..."

As part of this plan, CIRM will become increasingly multi-dimensional and deploy resources to address all of the relevant barriers standing in the path of accomplishing our mission. This should not be confused with a decrease in focus. It is not. In fact, we will be more focused on accomplishing our mission. However, we must recognize that there are very real factors beyond the scientific (e.g., regulatory, commercial, etc.) that stand in the way of stem cell treatments becoming a reality in the practice of everyday medicine. We need an approach that addresses all of these barriers. The use of the word "attacks" emphasizes the seriousness of our patients' medical needs and signifies our commitment to fight for them until we are successful.

"...meaningfully affecting the speed, probability and sustainability..."

Speeding up the development of treatments and improving their likelihood of success are central to the CIRM mission. The word "sustainability" was included because it is pivotal to the long-term well-being of current and future patients.

"...of stem cell treatments..."

The feedback from stakeholders was unambiguous and consistent with Proposition 71: CIRM should be focused on treatments dependent upon stem cells for their therapeutic effect.

"...to successfully help patients in need."

That CIRM exists, above all else, to help patients with unmet medical needs is both self-evident and worthy of reiteration.

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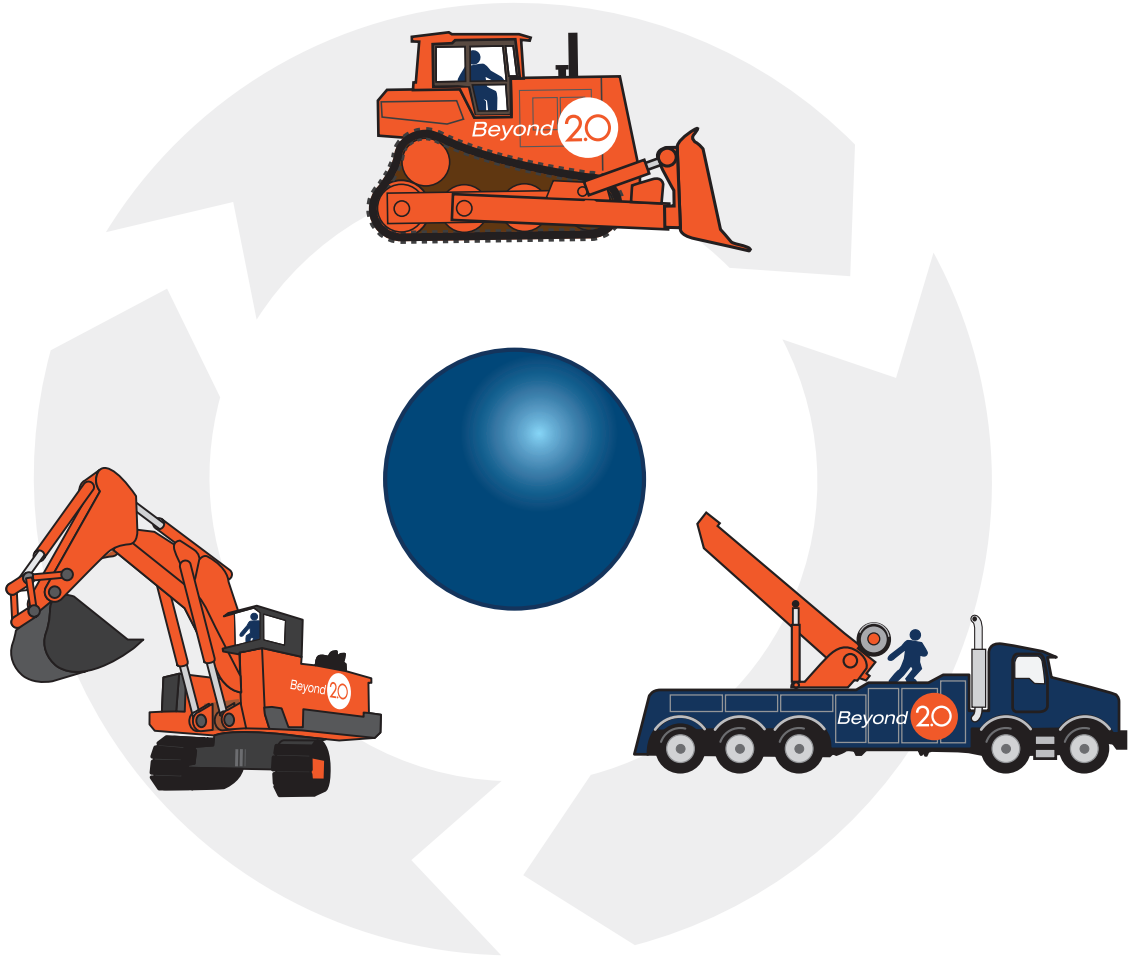
now it's personal

6 Strategic Themes

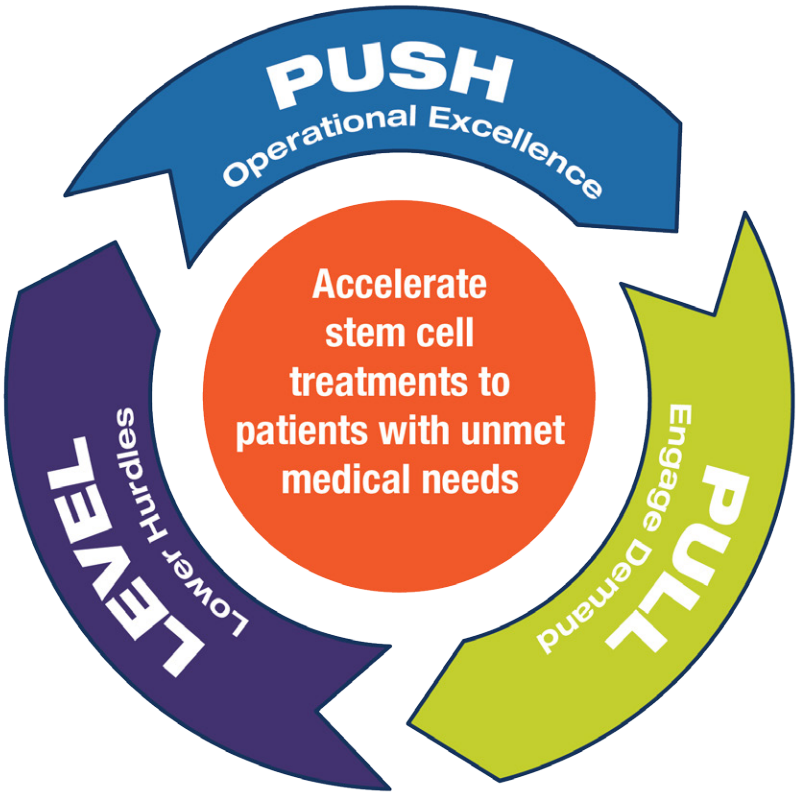


MISSION | To accelerate stem cell treatments to patients with unmet medical needs.

6 Strategic Themes

With the overriding vision established, it is time for us to move to the next level of detail – Strategic Themes. Although not an operational plan, to be most effective in the relatively short time remaining under the current funding initiative, it is important that this plan not stop at a theoretical, broad brush outline. Instead, it provides specific and tangible details that can be implemented and whose progress can be objectively measured. That way the CIRM team, the Board, and external stakeholders can maximize the utility of the plan as a tool and resource.

This plan has three Strategic Themes intended to work synergistically to accomplish the mission: Push, Pull and Level.



6 Strategic Themes

To use an analogy, CIRM is attempting to move a large boulder (stem cell treatments) over a mountain (development hurdles) to the valley on the other side (patients in need).

PUSH

Achieve Coordinated Operational Excellence

CIRM will attack this challenge with the three Strategic Themes of Push, Pull and Level.

First, CIRM will achieve operational excellence, our first Strategic Theme, by creating a stem cell treatment "pushing" machine. We will create our own unique machine, the Stemcelerator! While the Stemcelerator has specific components that will be described in greater detail later in the plan, the commonality among its parts is that they act in a strong, coordinated manner to drive stem cell technologies forward. They are, in fact, many of the "pushing" activities that have been at the core of CIRM since its inception.

So what is different now?

First, we will fully operationalize CIRM 2.0. With the recent addition of the CIRM 2.0 Discovery and Translation Programs to the existing Clinical Program, a solid backbone (or chassis) of linked programs now exists to support our machine. However, these programs, being brand new, will need to be refined and optimized to reach their full potential. With experience and commitment to continuous improvement, over time, these programs should not just meet, but exceed their current expectations.

Next, we will add critical infrastructure that will help accelerate historically slow and challenging portions of the development pathway. This new infrastructure will address the challenges unique to stem cell treatments that involve safely advancing promising new ideas from the research stage into clinical trials, which currently takes disproportionately more time when compared to non-cellular treatments.

Lastly, but perhaps most importantly, CIRM programs will no longer be independent and isolated initiatives. Instead, all of the "pushing" activities at CIRM (existing and new) will be linked and synchronized so that they work in concert toward the same goal. Also gone will be the uncertainty around when and how often our programs will be open for applications. All recurring programs will run according to a pre-defined schedule. Thus our applicants can prepare the best proposals possible, knowing CIRM will be there when they are ready. The goal is to take full advantage of the synergy that comes with a coordinated, team effort.

With these combined efforts, we hope to build and operate the world's most productive stem cell "pushing" machine, California's own Stemcelerator.

6 Strategic Themes

PULL

Engage Downstream Demand

Our second Strategic Theme is to recruit more downstream stakeholders to help accomplish our mission. In general, stem cell treatments have not yet captured the intense interest of the pharmaceutical and biotechnology industries or venture capitalists to the same extent as other classes of therapeutics. Similarly, there is not the same efficiency in pulling stem cell treatments from early stage research into more translational activities as exists for traditional pharmaceuticals, such as small molecules.

This lack of "pull" created an asymmetry in the development continuum of stem cell treatments that disproportionally hinders the pushing efforts of CIRM. While much of this effect can be explained by regulatory challenges or the differences in business models that arise when the therapeutic is a stem cell treatment, part of this imbalance appears to be tied to a lack of usable information available to potential collaborators. Under this plan, CIRM will initiate programs that actively connect various sources of downstream demand with our stem cell treatment technologies, thus shifting the "push-pull" equation in favor of more progress.

6 Strategic Themes

LEVEL

Lower Development Hurdles

The last Strategic Theme deals with regulatory burden. A striking 70% of CIRM stakeholders identified the FDA as the number one impediment to achieving the mission. Perhaps this is because there have been no stem cell treatments approved (nor are any near approval) in the United States despite the conduct of stem cell clinical trials for more than two decades. While effective regulation and oversight of all therapies, including stem cell treatments, is clearly necessary and desirable to protect patients' interests, stem cells present unique challenges that the current regulatory paradigm does not adequately address.

Several aspects of the regulations related to the development of stem cell treatments for patients are ripe for reform.

Currently, requirements in the preclinical section of an IND lengthen the time spent before a stem cell treatment can move into small, safety trials in humans, without clearly providing any benefit. Another opportunity for reform is in the regulatory requirements for diseases affecting small numbers of patients or those in whom highly individualized treatments are necessary. Rare conditions and the need for highly personalized treatments are more likely to be encountered in regenerative medicine since stem cell treatment is particularly suited to address these types of conditions. In these circumstances the current regulatory requirements and associated costs are so prohibitive that clinical development is easily abandoned but most often never begun at all.

To help level this playing field, CIRM will work with the FDA and other stakeholders to create a more efficient development pathway for stem cell treatments. Other countries have recognized this issue and have already introduced sophisticated initiatives that can serve as a template.

CIRM does not oppose regulation nor does it support the abolition of regulation, but we do believe that the regulatory burden currently placed upon the development of stem cell treatments must more accurately reflect the potential risks and benfits of that treatment, balanced against the very real consequences of doing nothing.

7 Specific Actions

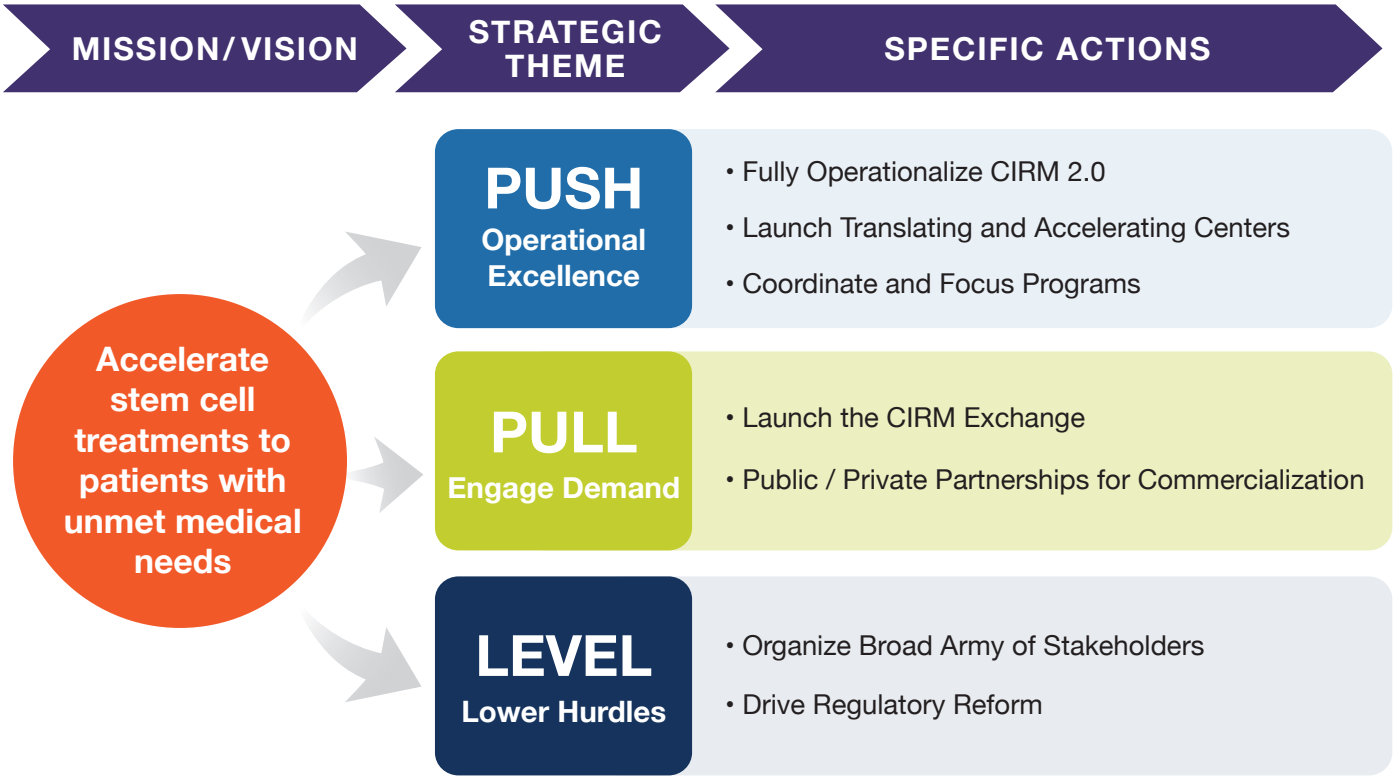
CIRM 2.0, a radical overhaul of the way the Institute conducts business.

MISSION | To accelerate stem cell treatments to patients with unmet medical needs.

Beyond CIRM 2.0 CALIFORNIA'S STEM CELL AGENCY

7 Specific Actions

The next level of granularity in our plan is the establishment of Specific Actions. Here we describe the activities that CIRM will undertake to support the Strategic Themes and in turn accomplish its mission to accelerate stem cell treatments to patients with unmet medical needs. The objective is to have every action traceable upstream to a Strategic Theme and downstream to Results, the latter of which can be measured both with respect to progress and ultimate outcome.

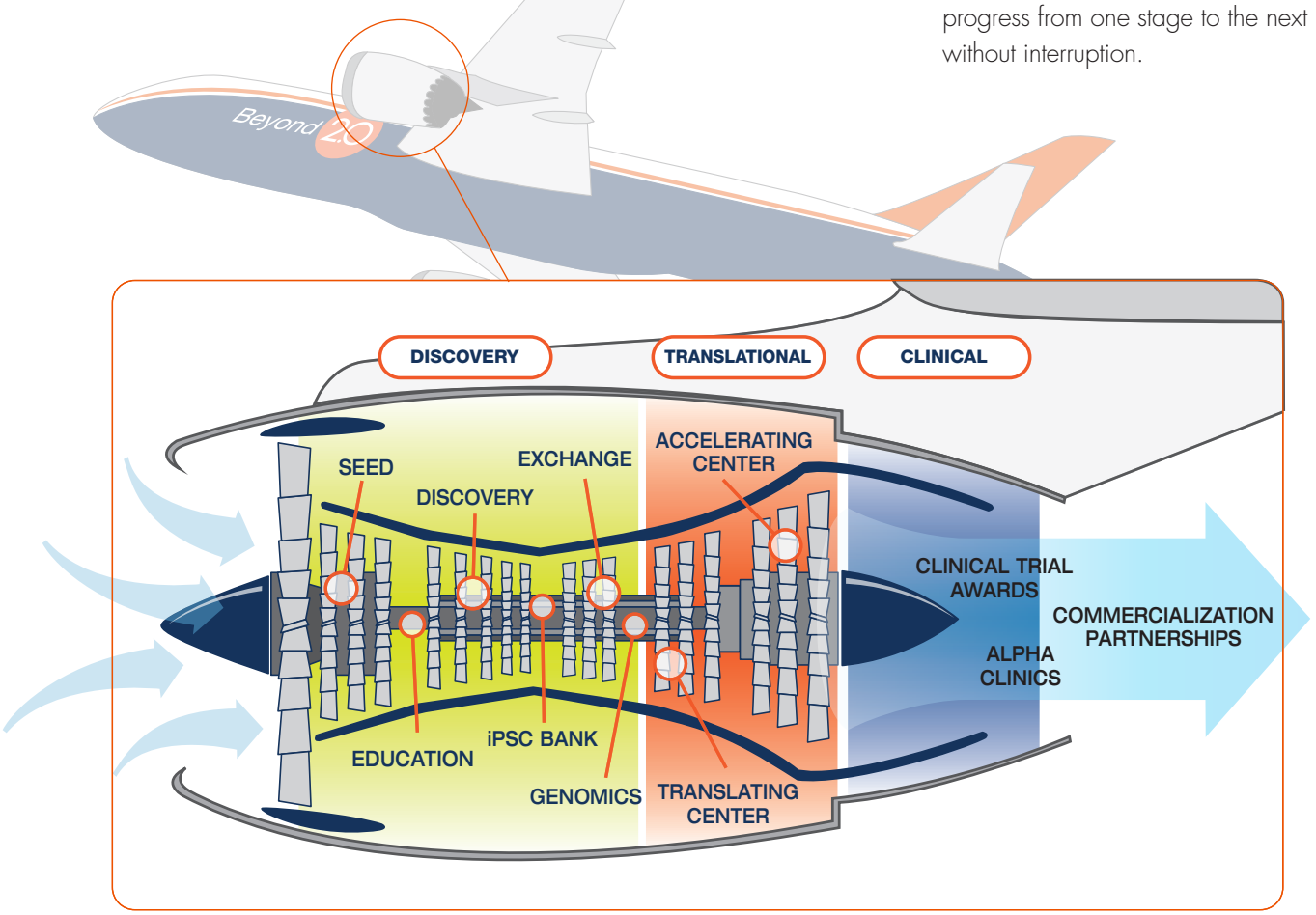


7 Specific Actions

Strategic Theme 1: Achieve Operational Excellence – PUSH

Specific Action:
FULLY OPERATIONALIZE CIRM 2.0

CIRM 2.0 is a radical overhaul of the way the Institute conducts business that implements efficient new systems which place added emphasis on coordination, speed, partnerships, and patients. The CIRM 2.0 Clinical Program has been operational since January 1, 2015, and, as described previously, is performing at or above expectation. The CIRM 2.0 Translational and Discovery Programs have been approved and are being launched. The full implementation of these CIRM 2.0 programs will create the chassis of a machine that provides a continuous, predictable, and timely pathway for the discovery and development of promising stem cell treatments. Execution is key as the introduction of CIRM 2.0 will benefit from both refinement and operator (CIRM) experience. Central to CIRM 2.0 functionality is the creation of linkages between stages of research, such that the product of each successful investment is the prerequisite for the next stage of development for the technology. With the adoption of CIRM 2.0 there are also now complete and continuous funding pathways to all potential successful outcomes of a project (therapeutic, device, diagnostic or tool). Finally, new award opportunities now happen according to a pre-defined schedule with each program type offered multiple times a year, allowing potential applicants the opportunity to prepare and file at the time most optimal to their project. Furthermore, these schedules are timed so that programs can progress from one stage to the next without interruption.



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7 Specific Actions

The operational success of CIRM 2.0 is built upon.

Coordination: With the adoption of CIRM 2.0, there are now complete and continuous funding pathways available for all potential successful project outcomes (therapeutic, device, diagnostic or tool). New award opportunities now happen according to a predefined schedule with each program type offered multiple times a year, allowing potential applicants the opportunity to prepare and file at the time most optimal to their project. Furthermore, these schedules are timed so that programs can progress from one stage to the next without interruption.

Speed: CIRM 2.0 seeks to speed up all aspects of how the Institute operates. From holding more frequent application review cycles to generating contracting templates, CIRM has been able to reduce the cycle time of its Clinical Program from 22 months to approximately 120 days. Timing of new awards and linkages means no down time. The Institute also realigned its financial payments to progress against a series of milestones established to drive timely performance. Disincentives to awardees completing their projects early have also been removed.

Partnerships: Under CIRM 2.0, the Institute does not act as a passive funding source, but instead is an active investor, devoting significant internal resources and leveraging its vast external team of world-class subject matter experts to advance the projects it selects. This creates a true partnership that accelerates projects and gives them the greatest opportunity for success.

Patients: Patients are at the heart of our mission and, accordingly, we make sure their input affects decision-making. Patient Advocates of the GWG are now assigned to the review of every application. After approval, each clinical project will be partnered with a project-specific Clinical Advisory Panel (CAP) to guide it forward. Importantly, every panel will include at least one patient advisor with first-hand experience of the specific condition, who will provide input, recommendations and the appropriate sense of urgency that can only come from the perspective of someone living with the disease.

7 Specific Actions

CIRM 2.0 Core:

In addition to the overhaul of research and development activities, CIRM's general operating activities (accounting, legal, HR, etc.) are being updated and refined to reflect current best practices necessary to accomplish CIRM's mission. This process, termed "2.0 Core" will ensure that the Institute operates in a manner that is both efficient and responsive.

One of the greatest benefits of moving to a systems-based approach (vs. initiative-based) is the opportunity for improvement that comes with repetition.

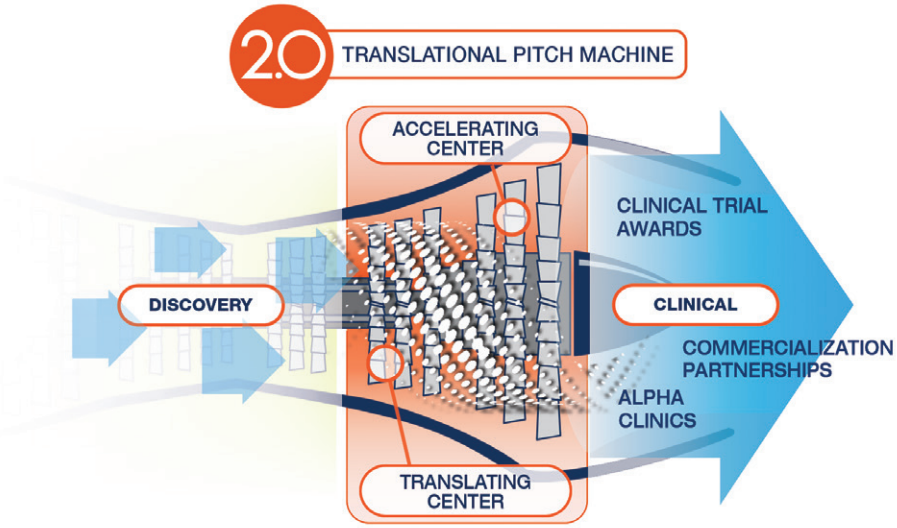
Continual Improvement:

One of the greatest benefits of moving to a systems-based approach (vs. initiative-based) is the opportunity for improvement that comes with repetition. Since all of the CIRM 2.0 programs are offered on a continual basis, it is expected that improvements to the process will be made with each passing cycle. To fully realize this opportunity, however, CIRM must be vigilant for opportunities to improve. Identifying opportunities and implementing continuous, objective measurement is critical. CIRM must also be willing to honestly confront program deficits and take prompt action for improvement.

Mission Critical Infrastructure (The "Pitching Machine")

To address the challenges that currently slow progress of translation of laboratory-based stem cell research to high quality clinical trials, CIRM is proposing two new strategic infrastructure programs (1) the Translating Center and (2) the Accelerating Center. The Translating Center and the Accelerating Center are designed to complement each other and work synergistically to support CIRM-funded Translational and Clinical projects. The Translating Center, a stem cell-specific preclinical research organization, will support IND-enabling activities while the Accelerating Center, a stem cell-specific clinical research organization, will support IND submissions and clinical trials.

CIRM intends to coordinate the efforts of these two programs with the existing Alpha Clinic program, which will be recommended for expansion if it continues to demonstrate value. Additionally, CIRM is evaluating adding a physician stem cell fellowship component to the Alpha Clinics Network.



It is very important to note that these two centers are designed to address common concerns that were raised by **both researchers and regulatory officials**, making them particularly valuable tools to increase the quality and speed of translational stage projects.

7 Specific Actions

Translating Center

Under this program, a single applicant organization will be funded to form the Translating Center, a top quality preclinical research organization with a proven track record of providing current Good Manufacturing Practice (cGMP), compliant cellular product process development and manufacturing services. It will also be responsible for management of the preclinical data package suitable for inclusion in an IND to support clinical testing of the given cell product Operating from a facility permanently located within California, the Translating Center will provide preclinical research services to clients developing stem cell-based treatments, with an initial emphasis on CIRM-funded projects, and a business plan to extend the services to other clients in the future. The Translating Center will receive seed funding for five years.

Translating Center Services will include:

- Development of cGMP compliant cell manufacturing processes
- IND-enabling safety and toxicity studies
- Coordination with FDA and the Accelerating Center to support IND filings

Accelerating Center

Under this program, a single applicant organization will be funded to form the Accelerating Center, a top quality clinical research organization with stem cell-specific regulatory expertise, a proven track record of providing the required services on a contract basis, the capacity to support multi-center national and international trials, and a dedicated focus on stem cell treatment clinical trials. The Accelerating Center, which will be permanently located within California, will provide logistical, operational and consultative services to clinical trial sponsors and clinics in order to accelerate the regulatory review process and the conduct of high quality stem cell treatment clinical trials. It will have an initial emphasis on CIRM-funded projects with a business plan to extend the services to other clients in the future.

Accelerating Center Services will include:

- Regulatory management
- Clinical trial planning, operations and management
- Data management systems, biostatistics and analytics

7 Specific Actions

Strategic Theme 2: **Engage Downstream Demand – PULL**

PULL

Engage Downstream Demand

CREATE THE CIRM EXCHANGE

The objective of the CIRM Exchange is to better stimulate demand by encouraging and creating more investigator-to-investigator and investigator-to-organization linkages for the efficient and timely movement of research outcomes downstream to the next phase of development.

During every meeting with California's major biomedical research institutions, without exception, participants raised the need for a "clearing house" that could pair investigators with later stage partners who possess the appropriate expertise and interest to advance the project to the next stage of development, e.g., helping a successful basic science investigator find a qualified partner for the project's translational research phase. Similarly, a need for pairing investigators to industry or disease foundations was also voiced.

Researchers involved in different stages of development need an easy way to find each other - a place both to offer what they have and state what it is they need. The model for this type of social interaction is quite mature on the internet and more recently has infiltrated the majority of mobile device platforms. The CIRM Exchange will be a place for finding the connections needed while maintaining the ability to control the dissemination of confidential or proprietary information.

We envision that participation in the Exchange will engage meaningful downstream interest in CIRM projects and lead to more and faster progression of activities.

7 Specific Actions

Accelerating Therapeutics Through Public-Private Partnerships

ENGAGE INDUSTRY DEMAND

As described previously in the plan, there is currently insufficient interest from industry for stem cell treatment technologies to meaningfully impact their efficient advancement to the marketplace, where groundbreaking science can ultimately benefit the greatest number of patients. This program will shift that equilibrium by promoting industry involvement in stem cell treatments through the creation of public-private partnerships that advance high quality CIRM-funded stem cell technologies toward commercialization, and hence to patients.

The Accelerating Therapeutics through Public-Private Partnerships, or ATP3 Program, will provide continued funding for an aggregated group of existing CIRM projects approved by CIRM and selected by successful industry applicants proposing to invest significant sums of capital for the operation of stem cell treatment companies in California.

It is important to note that no CIRM funds will be used for the establishment or operation of the entity. CIRM funding will only be used to supplement the continuation of research and development activities for successful projects that already exist within the CIRM portfolio.

7 Specific Actions

ENGAGE INDUSTRY DEMAND

The aggregation of a basket of otherwise unpartnered CIRM projects offers the successful applicant "multiple shots on goal." This increases the probability of successfully developing and commercializing a stem cell treatment, and makes significant industry investment in stem cell technology more attractive. The program also benefits other important stakeholders:

- **For Researchers –** continued funding for the advancement of their CIRM project.
- **For Universities –** demand creation for the out-licensing of CIRM-funded technologies with a greater opportunity to achieve a financial return due to the aggregation of risk.
- **For Citizens of California –** the creation of an industrial stem cell treatment powerhouse that expands the tax base, adds high quality jobs, and increases the likelihood of the commercialization of stem cell treatments for patients with unmet needs.

Successful applicants will demonstrate their commitment to the continued research, development, and commercialization of CIRM projects by:

- creating an exceptional business plan that describes the synergies they intend to realize through their technology aggregation strategy,
- assembling a top-tier leadership team with the skill set necessary to successfully execute the business plan, and
- securing the significant investment capital necessary for long-term success.

Consistent with CIRM 2.0 principles, the Institute will bring to bear both its internal resources and vast external team of world-class subject matter experts to actively advance the projects being funded. The result of a successful ATP3 program will be the formation of a true public-private partnership that accelerates the various projects selected and gives them the greatest opportunity to truly benefit patients in need.

7 Specific Actions

Strategic Theme 3: Lower Development Hurdles – LEVEL

Specific Action:
LOWER DEVELOPMENT HURDLES

Army of Stakeholders

As mentioned in Section 3, a consistent theme emerged from our outreach to stakeholders – people personally affected by a serious disease or condition have a strong interest in actively participating in advancing the CIRM mission.

CIRM intends to take advantage of this highly motivated community in the following three ways:

1. Increasing awareness of CIRM – CIRM benefits from heightened awareness generated by patient advocacy in two ways. First, by increasing the number of applications CIRM receives for its Clinical Program, and, second, by facilitating the dissemination of information leading to increased participation in clinical trials.

2. Participation on Clinical Advisory Panels – CIRM has recently instituted a new "Clinical Advisory Panel" (CAP) process that establishes small, dedicated groups of experts to shepard each of our clinical stage projects. The mission of each CAP is to afford every CIRM-funded clinical project the greatest chance of success. Central to this effort will be the inclusion of at least one patient representative on every panel for every project.

3. Advocacy for Leveling Development Hurdles – CIRM will identify patient advocacy communities alongside other stakeholder groups that are highly motivated to affect positive change in regulatory paradigms. CIRM intends to engage and educate these communities to enable them to be maximally effective at disseminating and advocating for regulatory reform to the larger patient advocacy community, the public, and other relevant stakeholders. As a united team, we intend to advance regulatory reform by working with and inspiring the necessary bodies, including Congress and the FDA, to bring about changes that will accelerate clinical testing and approval of safe and effective stem cell treatments, particularly treatments for patients with rare and unmet medical need.

7 Specific Actions

LOWER DEVELOPMENT HURDLES

Regulatory Optimization

CIRM does not oppose the regulation of stem cells by the FDA but is concerned about the lack of progress that has been made in the area of stem cell therapy. Since the current regulatory paradigm was enacted 15 years ago no stem cell product has been approved by the FDA. While there are those developing innovative treatments who are attempting to navigate the process, CIRM is particularly worried about the potential breakthroughs that are abandoned or never attempted because the regulatory pathway is viewed as prohibitive. It is not that CIRM believes the current path represents an impossible challenge but for many indications the time and cost associated with the current paradigm are unworkable. This is particularly true for rare diseases and treatment approaches that are highly personalized.

CIRM intends to work with the FDA and other stakeholders to improve the regulatory environment and in so doing increase both research and commercial interest in stem cell treatments.

Specifically, CIRM intends to:

- Partner with the FDA, our proposed Translating and Accelerating Centers, and our Grants Working Group to manage translational research more efficiently, leading to expeditious and higher quality IND submissions.
- Work with the FDA and other stakeholders to develop a more progressive, "tiered" approach to the regulation of the development of stem cell treatments.
- Identify practical tactics for significantly lowering the time and cost of developing treatments for rare conditions.

When successful, CIRM will help the United States develop a regulatory paradigm that will keep it competitive in the world market place and foster innovation for those patients who need it most.

7 Specific Actions

LOWER DEVELOPMENT HURDLES

Regenerative Medicine Needs the Tiered Approach That The FDA Promised

In 1997 the FDA announced new regulatory plans for human cells, tissues, and cellular and tissue-based products. Under this new system (implemented in 2001) the FDA promised a progressive regulatory paradigm, where the "regulatory burden" was to be proportional with the needs of the particular cell therapy in question. Specifically, the FDA wrote:

- "Under this tiered, risk-based approach, we proposed to exert only the type of government regulation necessary to protect the public health"
- "The regulation of different types of human cells… will be commensurate with the public health risks presented"
- "These planned improvements will increase the safety of human cells… while encouraging the development of new products"

Unfortunately, the regulatory framework that exists today is far from the ideas expressed above, namely a progressive continuum based on a balanced assessment of benefit as well as potential risk. What has evolved instead is a binary system under which some forms of cell therapy (e.g., cells from corneal, cartilage, bone, and bone marrow) are permitted to be marketed with very little FDA regulation and can enter the market in a few months with minimal investment.

All other cell therapies are subject to a one-size-fits-all regulatory paradigm that lacks nuance and is estimated to take over a decade to complete at a cost of over a billion dollars. Ironically during the 15 years this pathway has existed no stem cell product has gained FDA approval thus the true time and cost of this pathway is unknown. CIRM must work with other stakeholders to help the FDA to fulfill the progressive regulatory paradigm they originally set out to enact.

FDA's "Tiered" Approach to the Regulation of Cell Therapy

Regulatory Hurdles	Products Deemed by FDA to be of Low Risk	Everything Else
Facility Registration	X	X
Safety Verification of Source Tissue/Cells	X	X
Good Tissue Practices Compliance	X	X
Mechanism Studies		X
Safety Studies in Animals		X
Efficacy Studies in Animals		X
Manufacturing Controls		X
Potency Determination		X
IND Submission		X
Phase I Human Trial		X
Phase II Human Trial		X
Phase III Human Trial		X
Biological License Application		X
Pre Approval Inspection		X
Post Marketing Commitments		X
Estimated Time:	3 Months	**>12 Years**
Estimated Cost:	$100,000	**>$1,000,000,000**

8 Expected Results

Plan goals, milestones, and program checkpoints for objective, measurable success

8 Expected Results

This section describes the Major Goals of the plan for the next five years. Additionally, progress metrics and milestones that serve as intermediate checkpoints are provided. Both are objective and measureable.

Major Goals

This plan lays out an ambitious roadmap for the acceleration of stem cell treatments to patients with unmet medical needs. If successful, over the next five years the following goals will have been achieved or exceeded. They are presented in an order that further reinforces the machine-like nature of the plan, where the goals are intended to complement and build upon one another.

- **Discover:** Introduce 50 new therapeutic or device candidates into development.
- **Advance:** Increase projects advancing to the next stage of development by 50%.
- **Refine:** Enact a new, more efficient regulatory paradigm for cell treatments.
- **Accelerate:** Reduce the time it takes a stem cell treatment to move from discovery into a clinical trial by 50%.
- **Validate:** Add 50 new clinical trials to the CIRM portfolio, covering at least 20 unique diseases or conditions, and including at least 10 orphan and 5 pediatric indications.
- **Partner:** Pair at least 50% of our unpartnered clinical stage projects with commercial partners.

Performance Metrics

During the next five years, performance metrics will enable us to evaluate our progress, check for unintended consequences, and make any necessary course corrections essential to achieving our major goals. Key to the success of this plan is for all members of the CIRM team to understand the specific roles they play in the organization's success and to track the performance of their functional area against the plan. For this reason, as part of the strategic planning process, each functional area within CIRM has developed its own team mission and performance metrics, fully supportive of the Institute. Most of these metrics are recurring and monitor the performance and efficiency of the machine, while a few areas have progress milestones for the initiation of new major programs. The performance metrics for each team are described in the following pages. CIRM will appraise each functional area and, based upon effectiveness, determine the actual value of the performance metric necessary to achieve the Major Goals. These metrics are designed to monitor the progress being made toward completion of each of the Major Goals of the plan.

8 Expected Results

Portfolio Development & Review (Review) Team

The Review Team's Mission is to: Select the highest quality projects efficiently and with unimpugnable integrity.

A Review Team Member's Role in CIRM's Success is to:

Build a world class team of expert reviewers and engage them to continuously improve performance and results

Conduct rigorous reviews that adhere to all applicable rules and that select for the most highly meritorious projects

Rapidly communicate objective information regarding funding opportunities and review process to stakeholders

The Review Team's Success Metrics are:

Review Timeliness: Percent of reviews held as scheduled

Clearance: Percent of applications fully dispositioned within a review cycle

Governance: Number of COI policy excursions per month

Response Time: Time from review to summary generation

Robustness: Percent of GWG recommendations overturned by the ICOC

Quality: Percent of operational milestones achieved

Finance: Percent to expense budget

8 Expected Results

Discovery & Translation (D&T) Team

D&T's Team's Mission is to: Identify new stem cell technologies with the greatest potential to improve patient care and drive their progression towards clinical use.

A D&T Team Member's Role in CIRM's Success is to:

- Identify and recruit the best, new, high-impact ideas to CIRM for review
- Maximize project outcomes by proactively addressing project challenges, providing expert advice to investigators, and promoting project focus and by ensuring timely termination of projects that cannot achieve their objectives
- Partner with investigators to seamlessly advance successful programs to the next stage of development with a goal of zero down-time

The D&T Team's Success Metrics are:

Development:	Percent of awardees that are first time applicants
Quality:	Percent of applications forwarded for review that are recommended for funding
Timeliness:	Percent of milestones hit on-time
Success:	Percent of awards that achieve the project objective
Advancement:	Percent of projects that advance to the next stage
Efficiency:	Research cost per objective (Discovery) or milestones (Translational)
Finance:	Percent to expense budget

8 Expected Results

Therapeutics Team

The Therapeutics Team's Mission is to: Find and develop innovative clinical stage projects and do what it takes to facilitate their success in the service of patients in need.

A Therapeutics Team Member's Role in CIRM's Success is to:

- Aggressively recruit the best preclinical and clinical projects with the highest likelihood of success
- Partner with investigators to give each project the best chance of achieving its objectives
- Drive successful projects onward seamlessly to the next stage of development

The Therapeutics Team's Success Metrics are:

Development:	Percent of awardees that are first time applicants
Recruitment Volume:	Number of applications forwarded for review
Timeliness:	Percent of milestones hit on-time
Success:	Percent of awards that achieve the project objective
Advancement:	Percent of projects that advance to the next stage
Partnering:	Percent of unpartnered projects that partner
Efficiency:	Research cost per milestone achieved
Finance:	Percent to expense budget

8 Expected Results

Medical Affairs & Centers (MA&C) Team

The MA&C Team's Mission is to: Provide critical infrastructure and operational support to eliminate bottlenecks inhibiting the delivery of stem cell treatments to patients.

A MA&C Team Member's Role in CIRM's Success is to:

Identify key needs and establish necessary CIRM Infrastructure programs to accelerate the progression of stem cell treatment development and commercialization

Increase visibility and access to CIRM's Infrastructure programs to patients, sponsors, and researchers

Find new ways to further integrate and leverage existing Infrastructure programs to advance CIRM's mission

The MA&C Team's Success Metrics are:

Timeliness: Time from concept plan approval to activity start-up of an infrastructure program

Value: Number of unique Accelerating and Value Add Resources (AVARs) produced by the Alpha Clinics Network

Progress: Number of stem cell clinical trials completed at an Alpha Clinics

Effectiveness: Number of funded stem cell projects, addressing human disease and/or therapeutic development, that are serviced by a CIRM Infrastructure program

Advancement: Number of projects arising from the genomics program that successfully progress to successful CIRM 2.0 funding

Quality: Number of users for iPSC bank

Finance: Percent to expense budget

8 Expected Results

Administration Team

The Administration Team's Mission is to: Deliver the talent, technology, and communications needed for CIRM to advance its mission.

An Administration Team Member's Role in CIRM's Success is to:

Recruit and retain top quality employees

and

Implement, support and maintain information technology (IT) systems and processes

Create the materials and provide the support and training to the science team to help them achieve objective success for all CIRM initiatives

Create a stronger patient advocate following

Support the Board

The Administration Team's Success Metrics are:

Human Resources Effectiveness:	Time it takes to hire new employees
Human Resources Quality:	Average length of time an employee stays
IT Quality:	Number of defects that make it into a product release
IT Effectiveness:	Percent of time the system is up and available to users
IT Timeliness:	Number of on-time deliverables
IT Efficiency:	Average time to resolve help desk tickets
Communications Effectiveness:	Number of new patient advocates actively working with CIRM
Governance Effectiveness:	Number of Board meeting documents posted with ten-day lead time
Finance:	Percent to expense budget

8 Expected Results

Legal & Grants Management (L&GM) Team

The L&GM Team's Mission is to: Support execution of CIRM programs by establishing effective policies, ensuring the fair and efficient review of applications, and applying our rules uniformly.

A L&GM Team Member's Role in CIRM's Success is to:

Establish clear and effective policies for the submission and review of applications and for the administration and oversight of awards and seize every opportunity to make established policies more effective and easier to understand

Support fair and efficient review of applications by the CIRM GWG and funding decisions by the Board

Ensure CIRM rules are fairly and uniformly applied to applicants and awardees

The L&GM Team's Success Metrics are:

Efficiency:	Time from approval to executed award contract
Robustness:	Percent ICOC approval of policy recommendations
Timeliness:	Percent of timely submission of awardee reports
Clearance:	Percent of awardee reports reviewed within 30 days
Quality:	Number of COI appeals
Effectiveness:	Time to resolution of COI appeals
Compliance:	Percent variance from Policy/SOP
Finance:	Percent to expense budget

8 Expected Results

Finance Team

The FinanceTeam's Mission is to: Support the financial needs of the CIRM machine.

A Finance Team Member's Role in CIRM's Success is to:

Develop and maintain a sustainable operating budget that supports strategic and efficient use of CIRM's resources

Effectively and efficiently manage CIRM's assets and liabilities

Develop and maintain accounting and procurement policies that establish internal controls and ensure reliable financial information

The Finance Team's Success Metrics are:

Quality: Percent variance (actual spending versus budget)

Efficiency: Time to review and approve award payments

Clearance: Time to review, approve and submit invoices to the Department of General Services, State Controller's Office (DGS/SCO) for processing

Effectiveness: Percent of travel expense claims in compliance with travel policies

Percent of invoices processed by DGS/SCO without correction

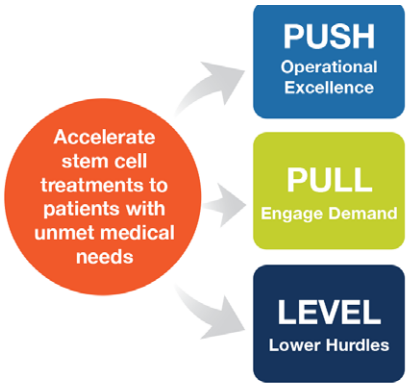
Finance: Percent to expense budget

9 Financial Summary

It is estimated that CIRM will be able to make approximately $890 million in new funding committments for the period from 2016 - 2020.

9 Financial Summary

Below is a high-level overview of the financial feasibility of the Strategic Plan, including some of the key assumptions that went into the model as well as estimated costs of certain programs. It should be noted that this is only a financial forecast and that adoption of this plan by the ICOC does not constitute a funding commitment for any given program or project. In fact, just the opposite. This plan is intended to give the ICOC more flexibility in adjusting spending priorities over time as certain needs arise or assumptions change.



Program	2016	2017	2018	2019	2020	Total
Education	10	10	10	10	10	50
Discovery	15	50	50	35	20	170
Translation	30	45	45	40	20	180
Clinical	90	100	100	100	50	440
Infrastructure	15	15	20	0	0	50
Totals	**$160**	**$220**	**$225**	**$185**	**$100**	**$890**

Financial Figures are in Millions

It is estimated that CIRM will be able to make approximately $890 million in new funding commitments for the period from 2016-2020. Currently, CIRM has $775 million in uncommitted funds on its balance sheet. The incremental $115 million is made up of funds that are or will be committed, but where the projects are reduced or discontinued prior to spending the full amount of the initial award. In such cases, the unspent funds are returned to CIRM and are able to be used for new awards. We have conservatively estimated this recovery rate to be approximately 10%.

Key Financial Assumptions:

- The "engine" is anticipated to be producing maximum power by 2017.
- $50 million previously committed by the ICOC for education (SPARK and Bridges programs) from 2016-2020.
- Translating Center estimated to cost between $12-15 million.
- Accelerating Center estimated to cost between $12-15 million.
- Recovery rate from cancelled projects expected to be approximately 10%.

10 Risks

Increased awareness of the problems we are likely to face will ensure we remain vigilant and are proactive in taking steps to prevent or overcome these problems.

10 Risks

The following list highlights certain risks identified by CIRM that could cause the Institute's actual results to fall short of this plan's projection. It is intended to heighten awareness of potential obstacles so that we can take proactive steps to prevent their occurrence and/or mitigate their effects. This list is not exhaustive.

There may be an insufficient number of meritorious treatments to reach our goals

CIRM is currently funding 15 clinical trials and a pipeline of more than 45 translational projects. Given the probability of success in biomedical research, CIRM needs to ensure a robust pipeline of translational projects in order to maximize its chances of succeeding in delivering treatments to patients. An insufficient number of translational projects with appropriate preclinical rationale to support demonstration of proof of concept in humans could jeopardize CIRM's chances of success. CIRM plans to address this concern by continuing to seed the pipeline at the discovery stage in order to maximize the opportunity for successful translational projects and by providing incentives to discovery researchers to push their discoveries to the next stage of research.

There may be insufficient interest from qualified applicants to participate in key competitions

Though CIRM intends to greatly increase the number of clinical trials and treatments in the Institute's portfolio, CIRM also intends to support only projects of the highest quality. The bar must not be lowered in order to achieve the strategic plan goals. In fact, as has been the practice under the CIRM 2.0 Clinical Program, CIRM intends to raise the bar for all CIRM programs in order to ensure that we fund only projects that have exceptional merit. Although CIRM will make every effort to identify and recruit promising, high caliber projects to California for partnership with the Institute, achieving the major goals in this area depends on the existence of such projects. It is possible that stem cell research is simply not advanced enough to support achievement of CIRM's target goals for the number of clinical trials and therapeutics candidates or that those projects are outside of California and the investigators are not interested in bringing their projects to California. CIRM plans to mitigate this risk by aggressively recruiting high quality projects and designing CIRM programs that are so compelling to drug developers that they are willing to relocate all or part of their projects to California.

10 Risks

The current limited funding of the Institute could affect the ability to retain or attract personnel

Although Proposition 71 did not provide a sunset date for CIRM, the Institute's life is limited by two related factors. First, Proposition 71 authorized CIRM to spend a total of $3 billion in bond proceeds. Second, of that $3 billion, CIRM may spend no more than six percent, or $180 million, plus donated funds and interest earned on its funds, for administrative purposes. In the absence of the authorization of additional funds or some alternative source of revenue, therefore, CIRM cannot continue to exist once its current funding expires. The uncertainty relating to CIRM's longevity creates a challenge for CIRM in recruiting and retaining talented team members. This challenge is compounded by the fact that the State's contribution towards an employee's retirement benefits vests after five years of service. Fortunately, CIRM has long benefited from the fact that its team members are drawn to the Institute because of its mission, not based on financial rewards. Nonetheless, CIRM is evaluating its policies to enhance its ability to attract and retain the top talent that the Institute has enjoyed since its inception.

Investors may be uninterested in stem cell treatments

To date, venture capital and the pharma and biotech sectors have been unwilling to make substantial investments in stem cell research. The lack of a track record of success, coupled with the regulatory uncertainty discussed above, have dissuaded them from making a substantial commitment to the field. This has exacerbated the challenges posed by the so-called "valley of death" between discovery and clinical translation where funding has traditionally been scarce. Although California voters made a substantial investment in CIRM when they approved Prop. 71, CIRM, by itself, does not have the funding necessary to translate the many discoveries made by researchers it has funded into treatments. Indeed, the costs of developing a single drug are estimated to be $2.6 billion. For CIRM to succeed in its mission, CIRM must partner with other investors to bring treatments to market and deliver them to patients. CIRM plans to address this concern by continuing to champion CIRM-funded project to potential partners and investors and by creating a demand for CIRM-funded projects through public-private partnership designed to accelerate treatment development, described in section 7 of this plan.

10 Risks

The FDA may be unwilling to improve the regulatory environment

Respondents to CIRM's strategic plan survey overwhelmingly identified the regulatory environment for stem cell treatments as the biggest roadblock to the field. The uncertainty of the regulatory pathway for stem cell treatments results in project delays and increased costs, and it dissuades investment in the field by venture capitalists, pharmaceutical companies, and the biotech sector. CIRM has established a working relationship with the FDA to address these concerns, but if the FDA is unwilling to take steps to improve the regulatory environment, it could remain a substantial obstacle to accomplishing CIRM's mission. To address this risk, CIRM is engaging in a dialogue with the FDA and other stakeholders about the opportunities for reform, including consideration of the Japanese model, or alternatively, other pathways such as the development of California-specific standards for the approval of stem cell treatments for use by patients in the State of California.

Stem cell treatments may not provide sufficient benefit to create enduring demand.

Advancements in medical research are generally measured by decades, not years, and on this time line, stem cell research is still in its infancy. When California voters approved Proposition 71, stem cell research offered great hope for the discovery of treatments and cures for patients with unmet medical needs, but scientists knew relatively little about the best ways to work with stem cells and convert them into mature cell types that would be useful as treatments. We have come a long way since those early days, and CIRM has been a major force in accelerating the rate of discovery in the field. Scientists have succeeded in coaxing skin cells into cells that act like embryonic stem cells, known as induced pluripotent stem cells (iPSC), and in deriving stem cell lines through somatic cell nuclear transfer (SCNT), but much remains unknown about the therapeutic benefit of stem cells. A lack of success in developing stem cell treatments that provide a therapeutic benefit beyond treatments that are currently available could lead to a lack of demand for, and investment in, stem cell treatments. The best way to mitigate this risk, of course, is to demonstrate the therapeutic benefit of stem cell treatments, a proposition to which CIRM is committed through its ongoing funding of the discovery pipeline.

A generalized stem cell-related safety concern may arise that impedes the ability to conduct clinical trials.

In 1999, a patient who was participating in a gene therapy trial at the University of Pennsylvania died during the trial, leading to a substantial set-back for the field of gene therapy. Fortunately, to date, stem cell clinical trials have not encountered similar challenges, but a generalized concern about putting cells into the human body could deter patients from participating in stem cell clinical trials. CIRM plans to address this risk by ensuring that the trials it funds are conducted with appropriate consent and under the highest standards, and if a trial encounters safety concerns, CIRM will take prompt action to address those concerns, including terminating the award if warranted. CIRM also intends to engage in education efforts to ensure that patients have complete information about potential clinical trials.