

# CURE

Beyond  
**CIRM** 2.0  
CALIFORNIA'S STEM CELL AGENCY  
*now it's personal*

## Strategic Plan

2016 & Beyond



# HOPE

# Table of Contents

- ① Introduction . . . . 1
- ② About CIRM . . . . 3
- ③ CIRM Today . . . . 9

CIRM 2.0 STRATEGIC PLAN

- ④ Mission Confirmation . . . 11
- ⑤ Vision For CIRM . . 10
- ⑥ Strategic Themes . 15
- ⑦ Specific Actions . . 19
- ⑧ Expected Results & Metrics . . . . . 28
- ⑨ Financial Summary . . . . . 30
- ⑩ Risks . . . . . 31

The diagram is a circular flow with three main segments: a blue 'PUSH' segment at the top labeled 'Operational Excellence', a green 'PULL' segment on the right labeled 'Engage Demand', and a purple 'LEVEL' segment on the left labeled 'Lower Hurdles'. In the center of the circle is an orange circle containing the text 'Accelerate stem cell treatments to patients with unmet medical needs'.

# 1 Introduction

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



# 1 Introduction

CIRM is undertaking 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 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 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.*



## 2 About CIRM

Proposition 71 arose from the people of California's desire to realize the promise of stem cell therapies 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 electorate 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 therapies 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 therapies 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 comprised of the three groups listed below.



### The California Institute for Regenerative Medicine

The Institute was established by the passage of Proposition 71 and held its first 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:

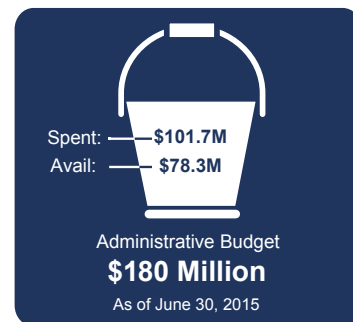
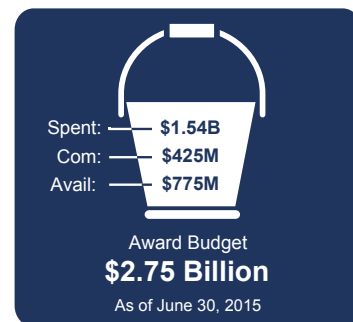
- establishing governance policies and structures;
- determining funding priorities;
- creating an application and review process;
- developing systems to manage review, award and finance processes; and
- creating an administration process to manage approved awards.

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.

## 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

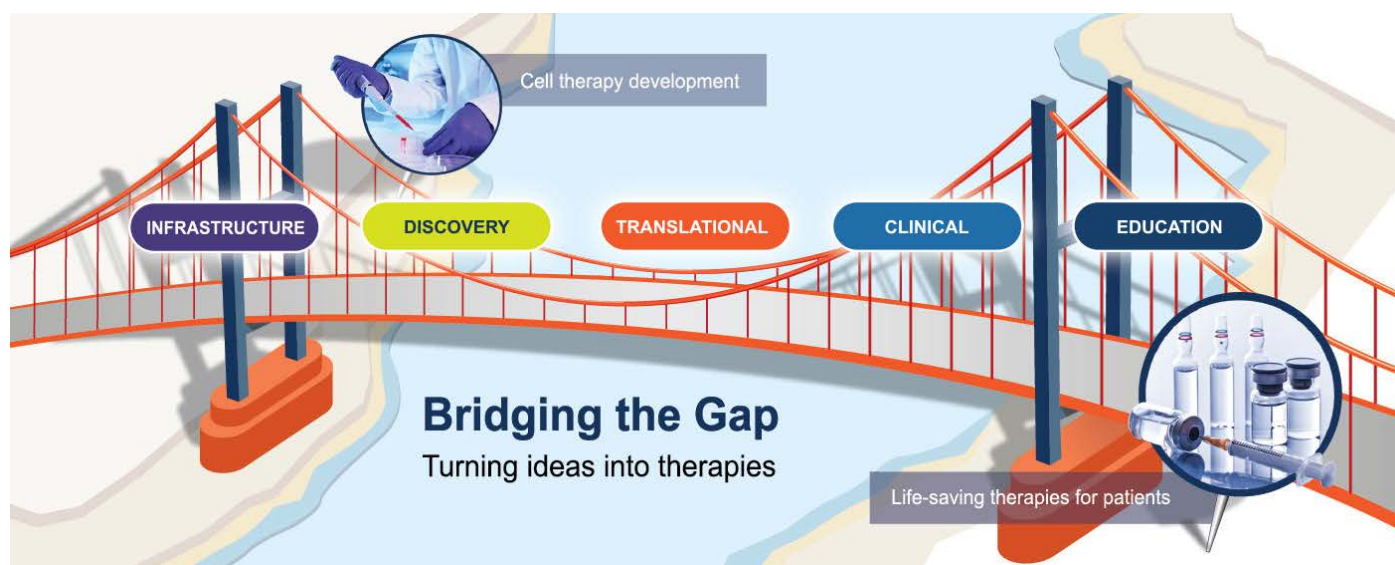
From 2006 through 2014, CIRM executed on its Mission through initiative-based funding wherein CIRM issued individual funding announcements describing a specific and singular scope of research and requesting the submission of applications responsive to those needs during a specified one-time submission 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 therapies 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



(formerly referred to as Basic Biology): The Discovery Program supports the exploration of new, potentially groundbreaking stem cell-based therapies and technologies from their inception through translation.

### TRANSLATION



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

### CLINICAL



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

# 3 CIRM Today

*It's a new day. CIRM 2.0 program  
reduces time for awards from 22 months  
to approximately 100 days.*

## 3 CIRM Today

Throughout our entire strategic planning process, we conducted significant field outreach to stakeholders in many forms. We held one-on-one meetings, visited academics centers, gained input from Board members, and listened to many patients and patient advocates. Overall, this information gathering process provided us with a broader and more external perspective to inform the discussions by those within CIRM. We spent much time absorbing, distilling, and synthesizing the information and what it meant for CIRM's future.

Five themes emerged that influenced every part of the resulting strategic plan. These learnings are described in the sections below.

### Initiative-based approach

It is easy to forget, but in the early days of CIRM, the field of cell therapy looked very different than it does today. While numerous diseases were being studied, the volume of research within each disease was much smaller than it is today, especially in translational, preclinical, and clinical development research. There simply was not adequate activity, nor resources within CIRM, to sustain programs designed to carry therapy development forward from a beginning to an ending point. Accordingly, CIRM was designed to function for a relatively lower volume of applications. This is what became an initiative-based approach, where we waited for critical mass to build in an area, released a request for applications (RFAs), and issued awards in response to the RFA. Then that RFA would be closed and it would be on to the next thing. This led to an opportunistic approach to research, however it was not predictable nor was it synchronous with other award programs. 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 of future funding opportunities.

Now that there is critical mass in the field, it is time to improve our process. A systems-based approach will allow us to create a continuum of research and development opportunities, with predictable and timely offerings, resulting in a more efficient process overall. In fact, 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 4 months today.

### Burden of Time for Translational Activities

Another commonly heard theme was the length of time needed to move a therapeutic candidate from preclinical to clinical development. Clinical develop-

ment can begin once an IND, or Investigation New Drug application is cleared by the FDA. This allows a therapy to be administered to patients in the clinical trials required for obtain regulatory approval. For a cell therapy, the average length of time to conduct the research and IND-enabling preclinical studies needed to submit an IND application is 8 years, compared to 3.2 years for traditional pharma and biotech drugs. Typically, the number of studies required is large and the duration of the preclinical studies themselves is long, contributing to the time burden. Furthermore, the FDA has applied the drug model of development to cell therapy, which oftentimes looks like forcing a round peg into a square hole, meaning the types of studies required and how to design and conduct them is not always optimized for cell therapy. In addition, inexperience among investigators and confusion as to exactly what is required for IND approval further lengthens the time to a successful filing. These clearly are opportunities for CIRM, with its resources and wealth of knowledge in this area, to play a larger, more impactful role.

# 3 CIRM Today

In the face of these challenges, many investigators with potential therapies are understandably deterred, and their therapies are delayed or sometimes never tested in the clinic. This needs to change to increase the flow of promising applications to CIRM for this stage of development and to improve the chances and accelerate stem cell treatments to patients with unmet medical needs.

## Minimal Industry Involvement

The third important learning from our research started with our own data. CIRM funds predominantly go to academia, with a disproportionately small share awarded to industry. In fact, 91% of CIRM dollars to date have been sent to academic institutions. While the research in academic institutions is of course critical to the development of novel, groundbreaking therapies, without industry involvement, there is no path forward for the large late stage clinical trials, manufacturing and product development needed to progress towards FDA licensure and ultimately, into the hands of physicians and patients. The lack of industry involvement is also reflected in the tech transfer offices at academic institutions. They told us that they present very few opportunities for cell therapies from their institutions to industry. Logically, it follows that very few licensing deals are completed.

We need to increase the awareness of industry regarding what CIRM has to offer and develop better ways to work with industry to accomplish our mutual goals of helping cures find their way to patients.

## FDA Challenges and Obstacles

We heard a resounding chorus from most stakeholders of the enormous challenges with the regulatory burdens placed on cell therapy in general, and stem cell therapy even more so, by the FDA. Instead of the ever growing body of work in cell therapy, with its overall excellent safety record, making the pathway to approval smoother, it seems to many that the requirements imposed by the FDA are increasing.

A recent therapy touted by the FDA as a success had such a high clinical development burden placed on it that by the time it was finally approved, standard of care had evolved and its market was significantly reduced, leading to liquidation of the company. Companies, and sadly patients, must go outside the United States, as far away as Japan, to find regulatory agencies willing to work successfully towards approval.

Ultra-orphan diseases still must reach the same statistical burden, which requires larger effect sizes than seen in the majority of approved, successful drugs and biologics. Everyone has their own list of how the FDA makes it seemingly impossible to take stem

cell therapy through the regulatory process. In 2014, Japan recognized the differences in regulatory approaches needed for regenerative medicine and took action. However, the FDA does not appear to have the same motivation. In fact, in a disturbing turn of events, FDA has recently begun providing certain members of the U.S. Congress with completely one-sided information on the dangers of cell therapies encountered in clinical trials. However, FDA failed to provide any context or balanced information regarding the safety record of cell therapies that comprises the vast majority published clinical literature. The FDA appears to be literally lobbying against the very therapeutic modality they are responsible for promoting.

CIRM needs to join with Congress, academia, and patients, to bring about real change to meaningfully balance risk-benefit in FDA regulations and more importantly, the FDA's behavior and willingness to grant licensure to effective therapies.

## Patient Advocacy Participation

The fifth and final theme is a desire 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 more to influencing CIRM's activities and direction. 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 with both its Board and external stakeholders.

The survey asked respondents:

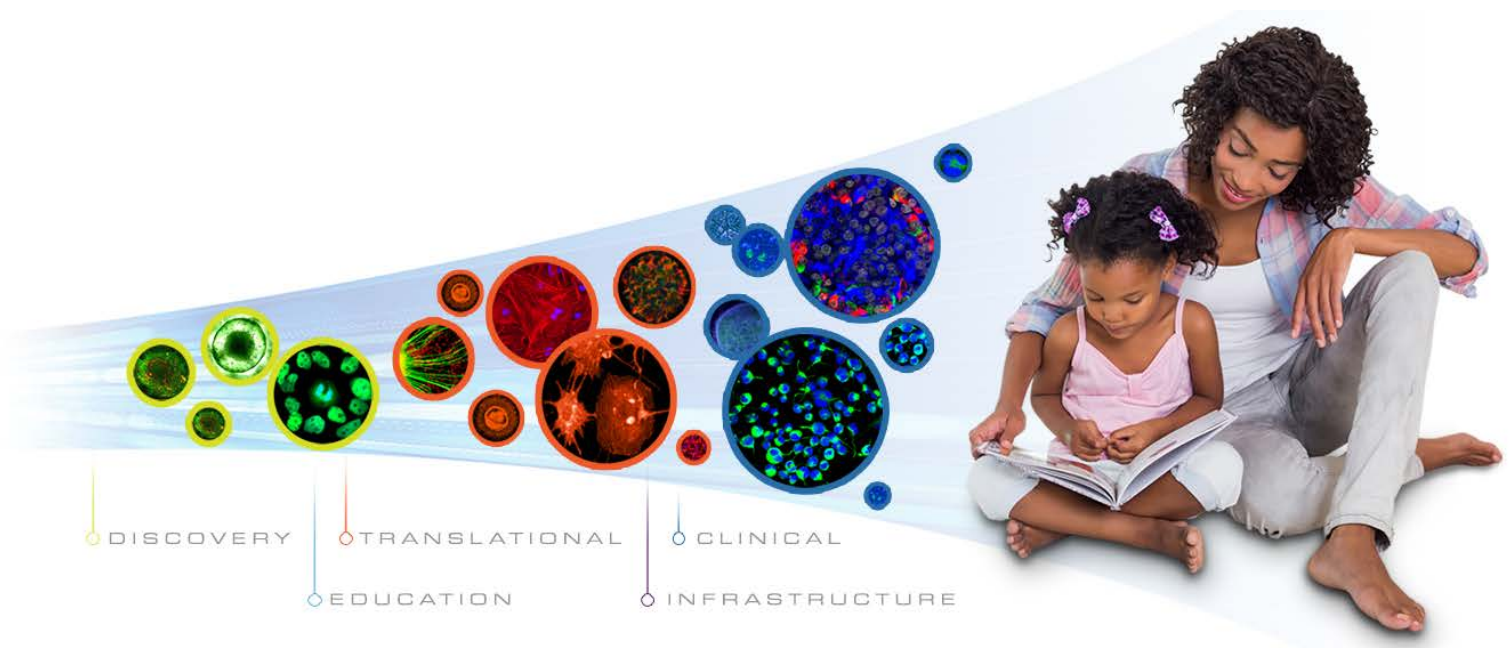
***Do you agree that the mission of CIRM should be "To Accelerate Stem Cell Therapies to Patients with Unmet Medical Needs?"***

The results were unequivocal. One-hundred percent (100%) of ICOC 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 as the point of orientation, we are able to move to the next level of detail on the plan – Vision. Specifically, what do 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.*

Examining the components of this statement allows us to provide a clearer understanding of its 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..."*

More leadership from CIRM was a recurring request made by many stakeholders and is a key component of this strategic plan. The cost of leadership is usually disproportionately diminutive when 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 address 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.

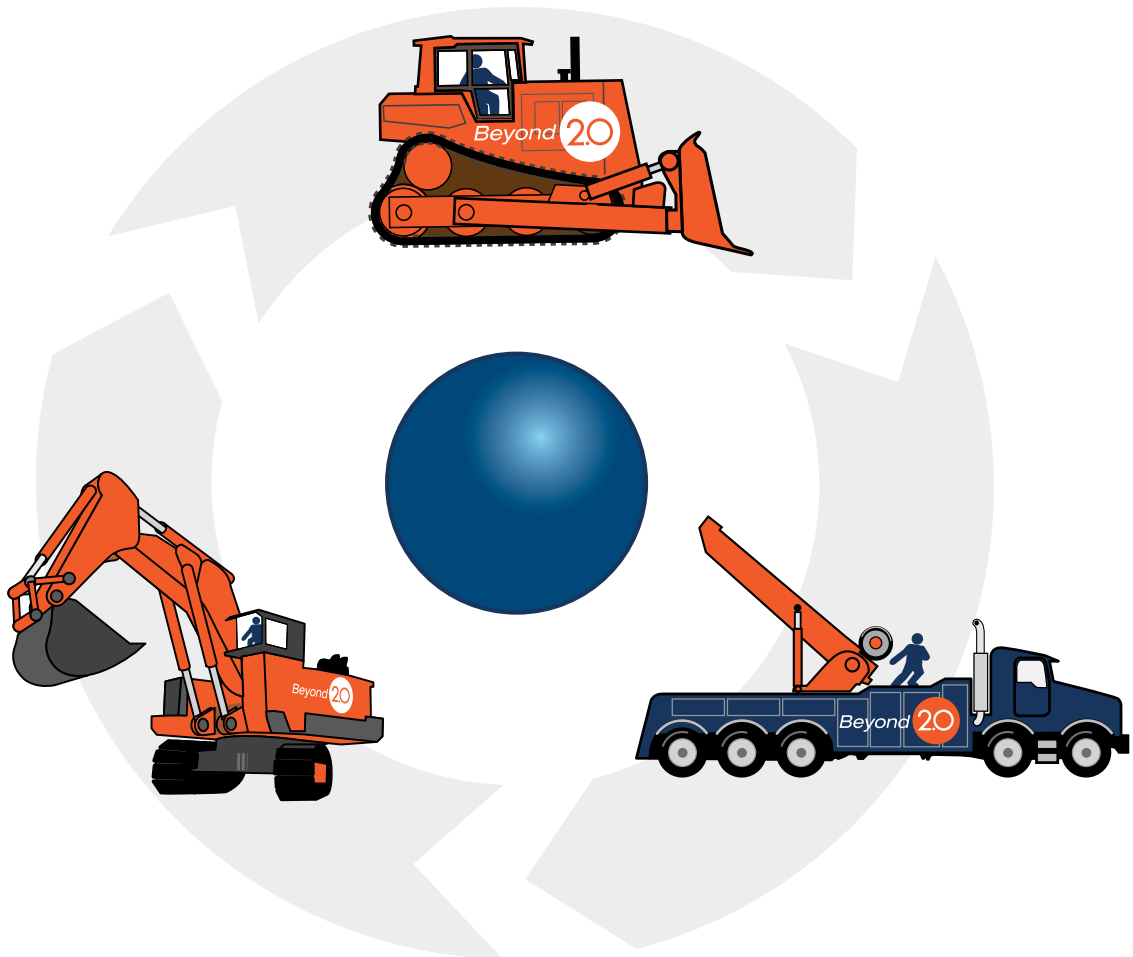
*"...to successfully help patients in need."*

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

20

*now it's personal*

# 6 Strategic Themes

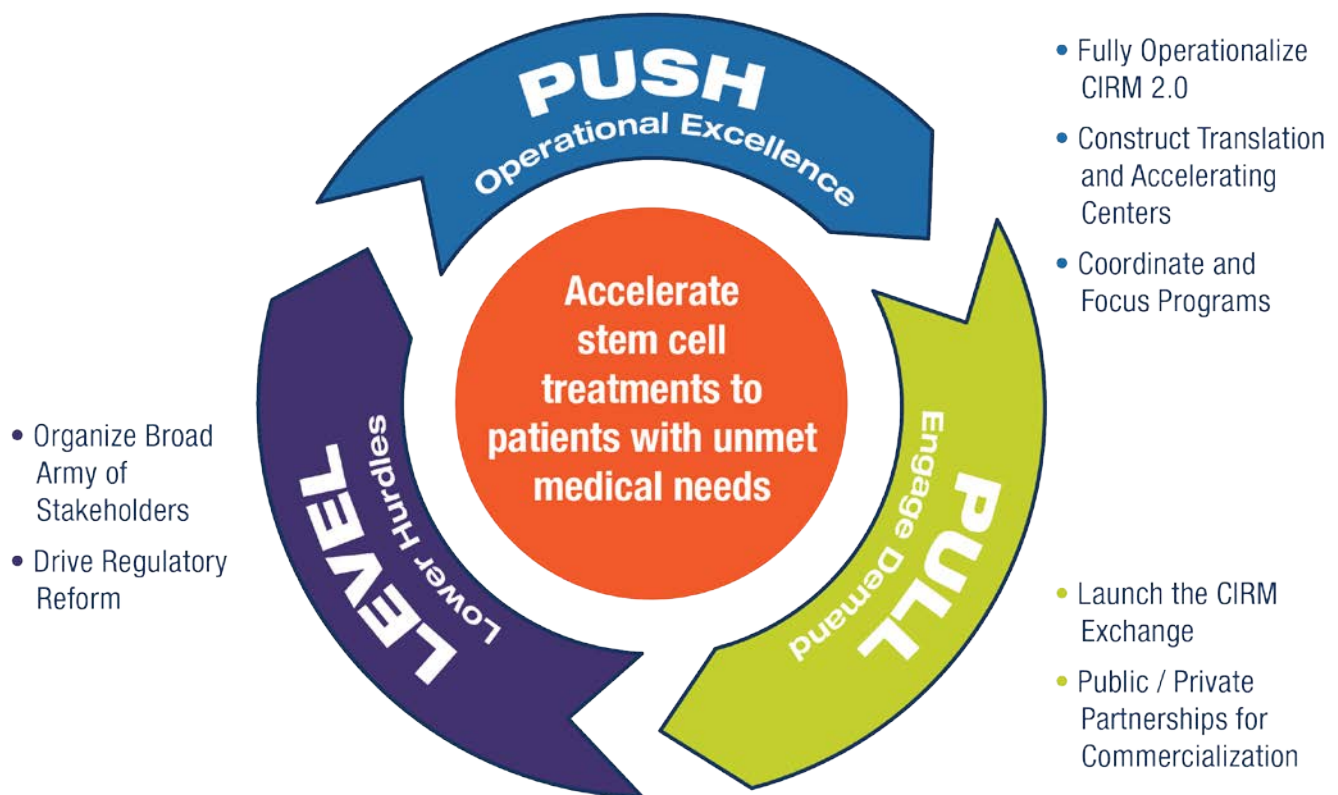




## 6 Strategic Themes

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 maximally 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 ICOC, 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 bolder (stem cell treatments) over a mountain (development hurdles) to the valley on the other side (patients in need).



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 therapy “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 on 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 cells therapies 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 therapies.

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 predefined 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 our mission. In general, stem cell therapies 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 cell therapies from early stage research into more translational activities as exists for traditional pharmaceuticals, such as small molecules.

This lack of “pull” had created an asymmetry in the development continuum of cell therapies that disproportionately 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 cell therapy, 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 cell therapy 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 U.S. Food and Drug Administration (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 stem cell therapies is clearly necessary, stem cells present unique challenges that the current regulatory paradigm does not adequately address.

Unfortunately, clouding this topic are a myriad of often opposing self-interests that make an easy solution elusive.

Despite all of the noise, two areas of stem cell regulation are clearly ripe for reform. The first is to address the non-value added requirements of the preclinical section of an IND (Investigational New Drug Application - permission from the FDA to conduct clinical testing on an unapproved therapy), which are currently unnecessarily lengthening the time spent before a stem cell therapy can move into small, first-in-man clinical trials. The second deals with how the current regulatory paradigm treats the clinical development of treatments for rare disease, which disproportionately affect stem cell based therapies.

To help level this playing field, CIRM will work with FDA and other stakeholders to create a pathway, especially for conditions that are both rare and serious. Other countries have recognized this issue and have already introduced sophisticated initiatives that can serve as a template and permit more rapid reform in the United States. FDA has initiatives that on the surface address the challenges of rare and serious diseases, but FDA's implementation still means an unfair and high burden on stem cell development and availability.

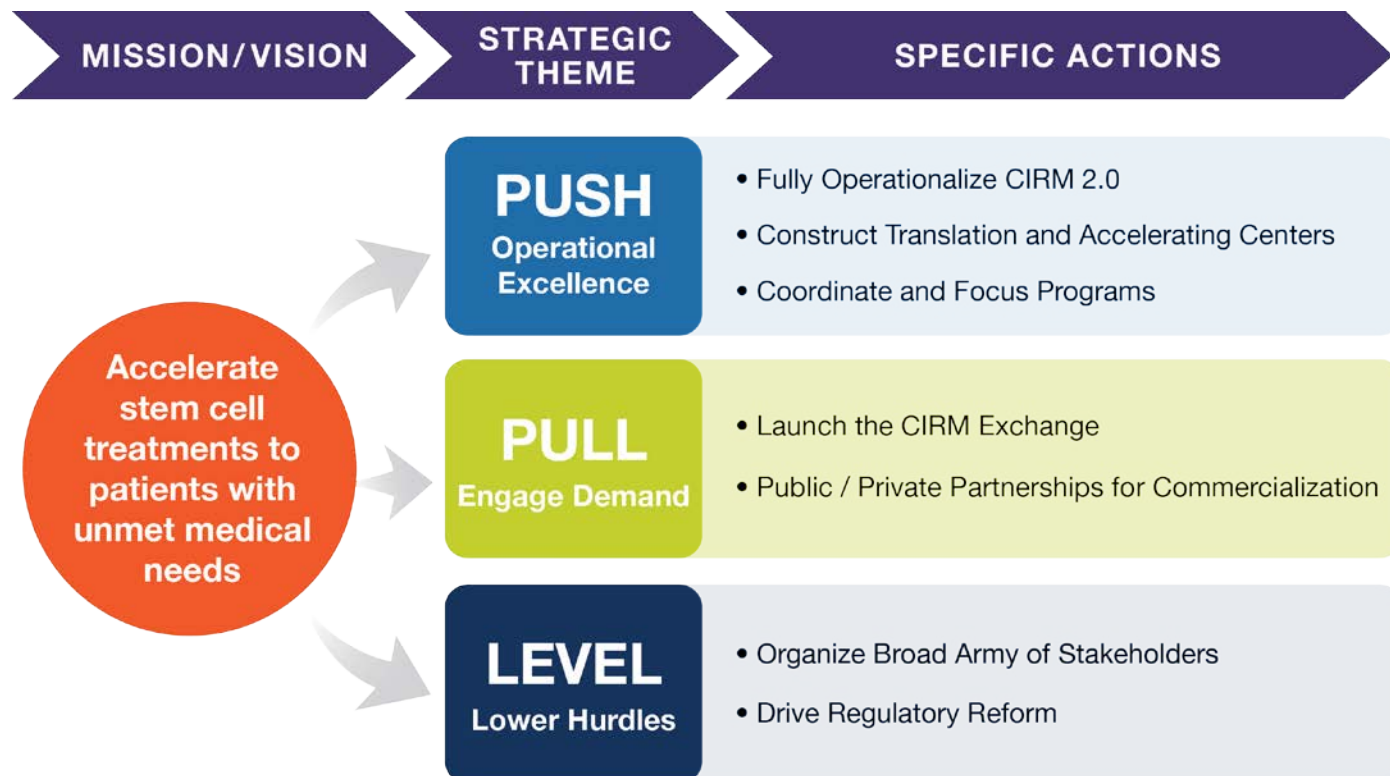
## 7 Specific Actions

*Fully Operationalize CIRM 2.0. A radical overhaul of the way the institute conducts business that places added emphasis on coordination, speed, partnerships, and patients.*



## 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

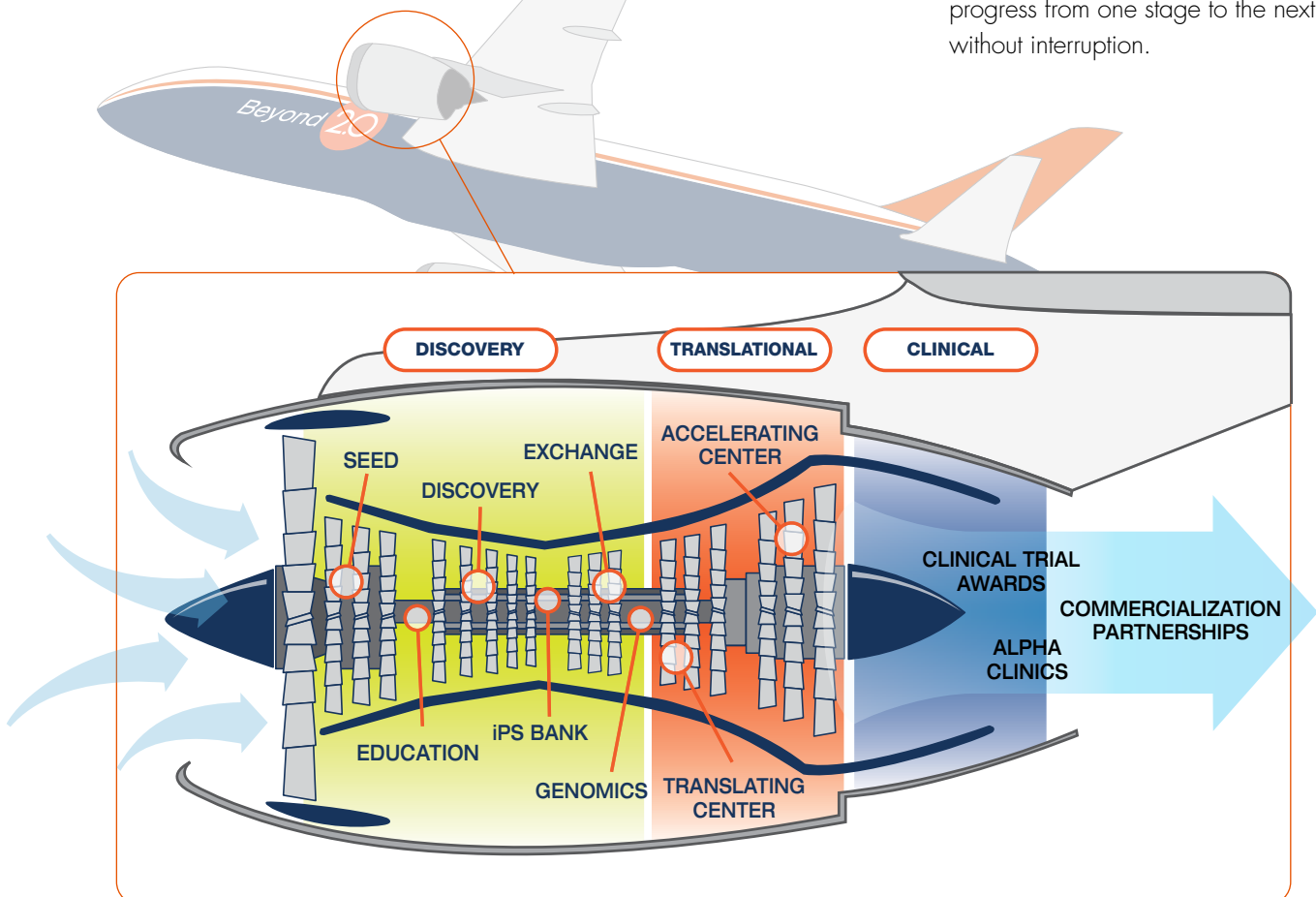
### Specific Action:

#### FULLY OPERATIONALIZE CIRM 2.0

CIRM 2.0 is a radical overhaul of the way the Institute conducts business that places 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-based therapies. 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 in the path

of developing 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 happened 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.



## 7 Specific Actions

CIRM 2.0 is built upon four basic concepts key to its success. These are:

**Coordination:** 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 investment in the development pipeline for the therapy or technology. With the adoption of CIRM 2.0, there are also now complete and continuous funding pathways available for all potential successful project outcomes (therapeutic, device, diagnostic or tool). Finally, 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 just 100 days. Timing of new awards and linkages means no down time. The Institute also modified its financial payments so they align with 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 true a partnership that accelerates projects and gives them the greatest opportunity for success.

**Patients:** Patients are at the heart of our mission and accordingly we are making sure their input affects decision-making. ICOC Patient Advocates are now assigned to the review of every application. After approval, each 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.

### Continual Improvement:

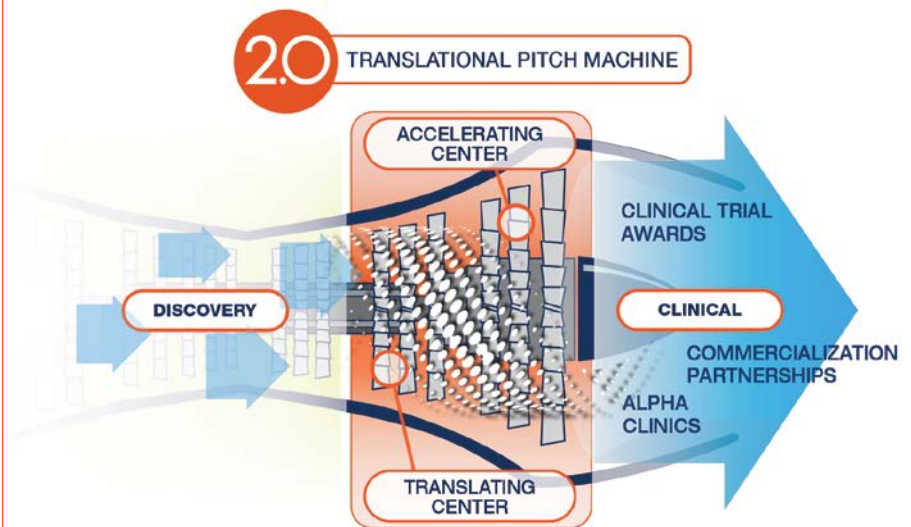
One of the greatest benefits of moving to a systems-based approach (vs. an initiative) is the opportunity for improvement that comes with repetition. Since all of the CIRM 2.0 programs are offered on a continual basis, it is expected that improvements to the process will be made with each passing cycle. 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.

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

### Mission Critical Infrastructure (The "Pitching Machine")

To address the challenges that currently slow progress from the translation of laboratory based stem cell research through 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.



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

## Construct 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 cGMP compliant cellular product process development and manufacturing services and 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 cell-based therapeutic candidates, 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 to provide core services to enable the issuance of an FDA Investigational New Drug (IND) application.

### Core 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 cell therapy clinical trials. Operating from a facility permanently located within California, the Accelerating Center 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 cell therapy clinical trials, with an initial emphasis on CIRM-funded projects with a business plan to extend the services to other clients in the future. The Accelerating Center will receive seed funding for five years to support IND submissions and clinical trials.

### Core 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 of research that has completed one stage of development

with investigators interested in taking the project through 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 of 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. It will be a space where participants will be vetted for authenticity prior to being released into the matching area.

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 cell therapy 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 cell therapy through the creation of

public-private partnerships that advance high quality CIRM-funded stem cell technologies toward commercialization.

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 cell therapy 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 therapeutic 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 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 will establish small, dedicated groups of experts to shepherd each of our clinical stage projects. The mission of each CAP is to afford every CIRM funded clinical trial the greatest chance of success. Central to this effort will be the inclusion of at least one patient representative on every panel for every trial.
3. Advocacy for Leveling Development Hurdles – CIRM will identify patient advocacy communities 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 on behalf of CIRM the plan 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 therapies, particularly treatments for patients with rare and unmet medical need.



# 7 Specific Actions

## LOWER DEVELOPMENT HURDLES

### Regulatory Optimization

The requirements for obtaining an IND is derived from classical pharmaceuticals and as such contains requirements that provide limited useful information for the initiation of Phase 1 clinical trials. However, these requirements are expensive and time consuming. Given that today, many critical go/no-go questions surrounding stem cell therapies can only be answered in human trials, CIRM intends to work with its various stakeholders and the FDA to remove non-value added activities from the preclinical requirements for an IND and pragmatically prioritize other activities by implementing a critical path approach so that they are conducted only when (and if) they are needed.

The treatment of rare diseases is another area that needs reform. This is an area important to CIRM in that stem cell therapies are particularly well suited for the treatment and cure of many of these diseases. Unfortunately, the time and expense of developing these treatments is disproportionately large when compared to the small size of the affected population and by extension the size of the market. Furthermore, the current paradigm significantly hinders the introduction of a therapy for a rare disease that offers an incremental improvement versus a cure. Our regulatory system should not discriminate against the development of safe and effective treatments, albeit not curative, simply because the underlying condition does not afflict the masses.

## 8 Expected Results

*Plan goals, milestones, and program check-points 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 check-points are provided. Both are objective and measurable.

### Major Goals



This plan sets forth 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 therapies.
- **Accelerate:** Reduce the time it takes a stem cell therapy 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, both of which are 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. Listed in the

following pages, are descriptions of the performance metrics for each team. CIRM will appraise each functional area and, based upon effectiveness, determine the actual value of the performance metric necessary to achieve the Major Goals. Holistically, 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:** Efficiently select the highest quality projects 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 And 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)

## 8 Expected Results

### Therapeutics Team

**The Therapeutics Team** Find and develop innovative clinical stage projects and do anything necessary to facilitate success in service of the patients in need.  
**Mission is to:**

#### 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

## 8 Expected Results

### Medical Affairs (MA) Team

**The MA 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 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 therapy 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 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

## 8 Expected Results

### Administration Team

**The Administration Team's Mission is to:**

Deliver the talent, technology, and communication 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  
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:

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



## 8 Expected Results

### Legal And 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

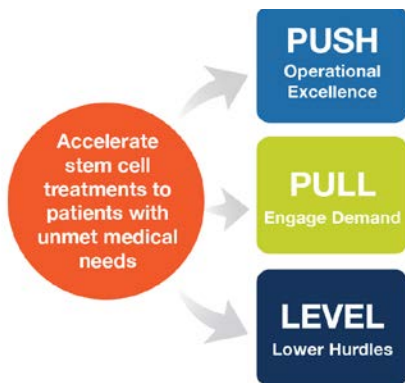
## 9 Financial Summary



*It is estimated that CIRM will be able to make approximately \$890 million in new funding commitments 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
<b>Totals</b>	<b>\$160</b>	<b>\$220</b>	<b>\$225</b>	<b>\$185</b>	<b>\$100</b>	<b>\$890</b>

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 canceled projects expected to be approximately 10%.

## 10

## Risks

*Heightened awareness of our potential obstacles will ensure plan vigilance, and proactive steps to prevent or mitigate their effects.*



# 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 therapeutic candidates 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 therapies 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 therapeutic candidates 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, CIRM'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 therapies

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 therapies. 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 therapies 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 therapy 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 therapies as the biggest roadblock to the field. The uncertainty of the regulatory pathway for stem cell therapies 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 therapies for use by patients in the State of California.

## Stem cell therapies 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 therapies 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 therapies. 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 therapies that provide a therapeutic benefit beyond treatments that are currently available could lead to a lack of demand for, and investment in, stem cell therapies. The best way to mitigate this risk, of course, is to demonstrate the therapeutic benefit of stem cell therapies, a proposition to which CIRM is committed through its on-going 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 setback 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.