SOMETHING BETTER THAN HOPE

Right now.

CIRM
CALIFORNIA'S STEM CELL AGENCY

2018 Annual Report
Every Moment Counts. **Don't Stop** Now.

Mission

Accelerate stem cell treatments to patients with unmet medical needs

With our help, good ideas have the power to transform medicine, lives and the future.

It takes commitment and courage to challenge what we've done before, to push ourselves harder, to always get better to fulfill our mission.

Because every moment counts.

Right now.

At CIRM, we never forget that we were created by the people of California when they approved Proposition 71 in 2004, authorizing $3 billion to fund stem cell research in our state.

To meet this challenge, our team of highly trained and experienced professionals actively partners with both academia and industry in a hands-on, entrepreneurial environment to fast-track the development of today's most promising stem cell technologies.

CIRM is focused on achieving its mission through the timely and efficient funding of high-quality stem cell projects and accelerating delivery of resulting treatments and cures to patients in need.

For more information visit, **www.cirm.ca.gov**

Dr. Tippi MacKenzie, above and on the front cover, is developing a technique to treat alpha thalassemia major, an often fatal blood condition. She performed the first in-utero stem cell transplant. See page 2 for more.

Dear Fellow Californians,

Looking back on 2018, I have been reflecting on our accomplishments, and I am in awe of how far we've come. Every researcher, clinical scientist, patient advocate and institution that we've supported should feel proud.

To date, we've invested nearly $2.6 billion in the potential of people. We've ensured that the great minds of this generation are supported and funded to shape the next frontier in medicine.

In 2004, when the voters of California entrusted us to spearhead the state-wide effort to expedite stem cell research, we never could have known that we'd successfully fund 50 clinical trials and support 1,000 projects.

But we are doing more than just funding the research that can lead to new treatments. We are also creating the infrastructure to deliver those treatments to patients in a safe and effective manner. Our unique CIRM Alpha Stem Cell Clinics Network gives patients access to cutting-edge therapies that are backed with solid science and delivered by experts in the field. Contrast this to the growing number of practitioners around the U.S. offering unproven and unapproved therapies that endanger patients and cost them thousands of dollars for treatments that have never been shown to work.

Our commitment to our patients and the people of California has helped us establish our state as a global leader in regenerative medicine.

This is, always has been, the promise of CIRM—taking the potential of stem cell research and turning it into reality. And we are delivering.

Jonathan Thomas

Jonathan Thomas, Ph.D., J.D.
Chairman, CIRM Governing Board

Dear Friends,

As we enter 2019, we are delighted by the increasing number of transformative medical treatments on the horizon made possible by CIRM.

Nearly 15 years ago, California taxpayers entrusted us with $3 billion to navigate the unknown, to bring stem cell science from the research lab to the bedside. Today, California is a leader in regenerative medicine, having built a robust ecosystem that has transformed the global research community.

CIRM's mission is to accelerate stem cell treatments to patients with unmet medical needs. Think about patients like baby Elianna on page 2. She was treated with stem cells for a life-threatening blood disorder while still in her mother's womb. Ronnie (page 15), who was born with what was previously considered a fatal immune disorder, is alive and thriving today. These stories inspire and motivate us to continue to build upon the great strides CIRM has already made.

As you will read in this Annual Report, CIRM programs have attracted significant industry partnerships and international involvement. The CIRM acceleration model is recognized by other organizations, including the National Institutes of Health, which joined forces with us to find a cure for sickle cell disease.

When we fund researchers, we are paving the way for treatments. When we support this work, we connect researchers, patients, patient groups, policymakers and investors across the country and around the globe.

At CIRM, we deeply respect the urgency of our mission and are committed to keeping our promise to accelerate stem cell treatments to patients, to relieve suffering and to improve the lives of millions of Californians and people around the world.

Every moment counts, and we will not slow down! Our resolve is stronger than ever.

Maria T. Millan

Maria T. Millan, M.D.
President and Chief Executive Officer

World's first in-utero stem cell transplant

Operating on a baby is always a delicate affair, but doing so while it is still in the womb involves the highest levels of skill and care.

University of California San Francisco's Dr. Tippi MacKenzie, a pediatric surgeon and researcher who was funded by CIRM during the early stages of basic research, has now developed a way to treat alpha thalassemia major, a blood condition that often results in fetal demise. In this novel technique, the baby is treated before birth.

Using Dr. MacKenzie's new approach, stem cells from the mother's bone marrow that have the power to become any kind of blood cell are introduced into the developing baby. These stem cells can then mature into healthy blood cells. In the womb, the baby's immune system is more likely to accept the mother's cells as its own.

Born in February 2018, Elianna is the world's first child to receive in-utero stem cell therapy to treat alpha thalassemia major. The information gained from this first-ever trial is an important step in finding a cure for babies with this fatal condition.

Better than hope, cures are inevitable

By creating CIRM, the people of California enabled us to work in ways no other state agency could, attracting the best science to the state with a goal of increasing access to cutting-edge medical advances for all Californians.

Today, California leads the emerging field of regenerative medicine, bringing forward therapies that have cured children from immunodeficiency diseases, improved function for paralyzed young adults and provided kidney and lung cancer patients a second chance at life. While once there was only hope, now we know that cures are imminent.

Better than hope, CIRM is driving cures today, right now, for some of the most challenging diseases and conditions, such as diabetes, blood disorders, blindness, paralysis and cancer.

Elianna and her mother, Nichelle Obar, following the world's first in-utero stem cell transplant, at UCSF in February 2018. Photo courtesy of Barbara Ries for UCSF.

Something better than hope.

Right now.

Breakthrough Approach

CIRM has created a new model for developing medical and scientific advancements.

Better than hope, CIRM's approach delivers results.

As a **state-funded** organization created to support programs and cures through cell-based regenerative medicine, CIRM is unique. By providing projects not only with funding, but also with **support, guidance, advice and expertise**, we have become an accelerator of medical science. Our **early funding** for promising science helps researchers show that their projects have potential, which gives venture capitalists and others the opportunity to invest in revolutionary science with confidence. What's more, patients and **patient advocates are embedded in everything** we do; they remind us every day why we do what we do, and why we can't stop now.

CIRM is the world leader in regenerative medicine. Our **strategic investments** in education, infrastructure and research initiatives (shown on the next page) create the framework for a new era in medicine. Our involvement in the **community** and with **public institutions** (like the National Institutes of Health) ensures public input. Working closely with **private industry** helps draw resources, talent and further investment to California.

Public

CIRM and the National Institutes of Health

In 2018, CIRM entered into a landmark agreement with the **National Heart, Lung and Blood Institute**, which will deploy CIRM's expertise, infrastructure and proven funding processes to financially support and accelerate the most promising regenerative medicine approaches to cure sickle cell disease, a condition afflicting 100,000 Americans and millions more worldwide.

NIH
National Institutes of Health

Private

Paving the way for private industry

CIRM's expertise helps "de-risk" young biotech companies and gives private funders the confidence to invest in them. For example, **Forty Seven Inc.**, based in Menlo Park, grew out of research from Stanford University and now is developing stem cell therapies for different forms of blood and solid cancers. The company has successfully secured follow-on funding and went public in 2018. Similarly, **Orchard Therapeutics** started with a CIRM-funded gene therapy program for severe combined immunodeficiency (SCID) as its lead program. It secured private investment, expanded its portfolio of gene therapies and established an office and manufacturing facilities in California. It, too, had a successful IPO in 2018.

FORTY SEVEN
Orchard therapeutics

Strategic Investments

CIRM supports education and research at various levels of development, from building infrastructure to clinical trials, that collectively form a unique regenerative medicine "ecosystem" in California.

Education

$110,000 in 2018
($219 million to date)

CIRM supports programs to train high school and university students—the next generation of stem cell scientists—to promote knowledge sharing, advance the field and build a pipeline of talent for California's stem cell industry.

Infrastructure

$0 in 2018
($482 million to date)

CIRM's infrastructure program builds real and virtual centers that provide the resources, expertise and information needed to efficiently advance CIRM's mission.

Discovery

$17.4 million in 2018
($905 million to date)

We support and invest in discovery (basic or early-stage research) that explores new and groundbreaking stem cell treatments and technologies.

Translational

$27.6 million in 2018
($343 million to date)

CIRM takes the best therapy candidates identified through discovery and supports them through the critical steps needed to advance toward the clinical development stage.

Clinical

$100.5 million in 2018
($647 million to date)

We are building a world-class therapeutics portfolio supported by unique resources to increase chances of success in the clinical phase of research. We fund the rigorous work necessary to get stem cell treatments ready for testing in patients in a manner acceptable to the Food and Drug Administration (FDA). Then we support the clinical testing of these treatments for safety and efficacy in patients.

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Right now.

Driving Industry and Investments

CIRM is building strategic partnerships through collaboration with private industry.

By putting our support behind promising research programs, CIRM has succeeded in bringing some of the best science to California, which has attracted significant additional scientific and commercial investments to the state.

From 2015 through 2018, private funders followed CIRM's lead and invested $1.64 billion in CIRM-supported projects. More than $1 billion was invested in 2018 alone, doubling all investments made in the three years prior.

In fact, $2.6 billion in CIRM grants to date has been leveraged to bring in an additional $3.2 billion in matching funds and investments from other sources.

Leveraged funds to date: $3.2 billion for CIRM-supported programs, past and present.

CIRM is a lender of first resort, supporting projects long before most investors are ready to come on board. Because of the credibility CIRM brings, those projects are now able to attract industry partners willing to invest hundreds of millions of dollars.

Co-funding:

Funding from institutions, industry or investors who join with CIRM to fund a specific project at the outset. (CIRM and partner funding are concurrent.)

$1 billion

Partnership Funding:

Disclosed support committed by partners independent of CIRM funding to help advance a project.

$1.6 billion

($1.06 billion in 2018)

Additional Funding:

Any funding a Principal Investigator can secure by leveraging CIRM's backing of the project to attract additional funds from investors.

$541 million

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$1.64 billion

New private funding has multiplied each year—from $40.5 million in 2015 to $1.06 billion in 2018.

Total private funding
2015–2018: $1.64 billion

2018 | **$1.06 billion**

2017 | **$389 million**

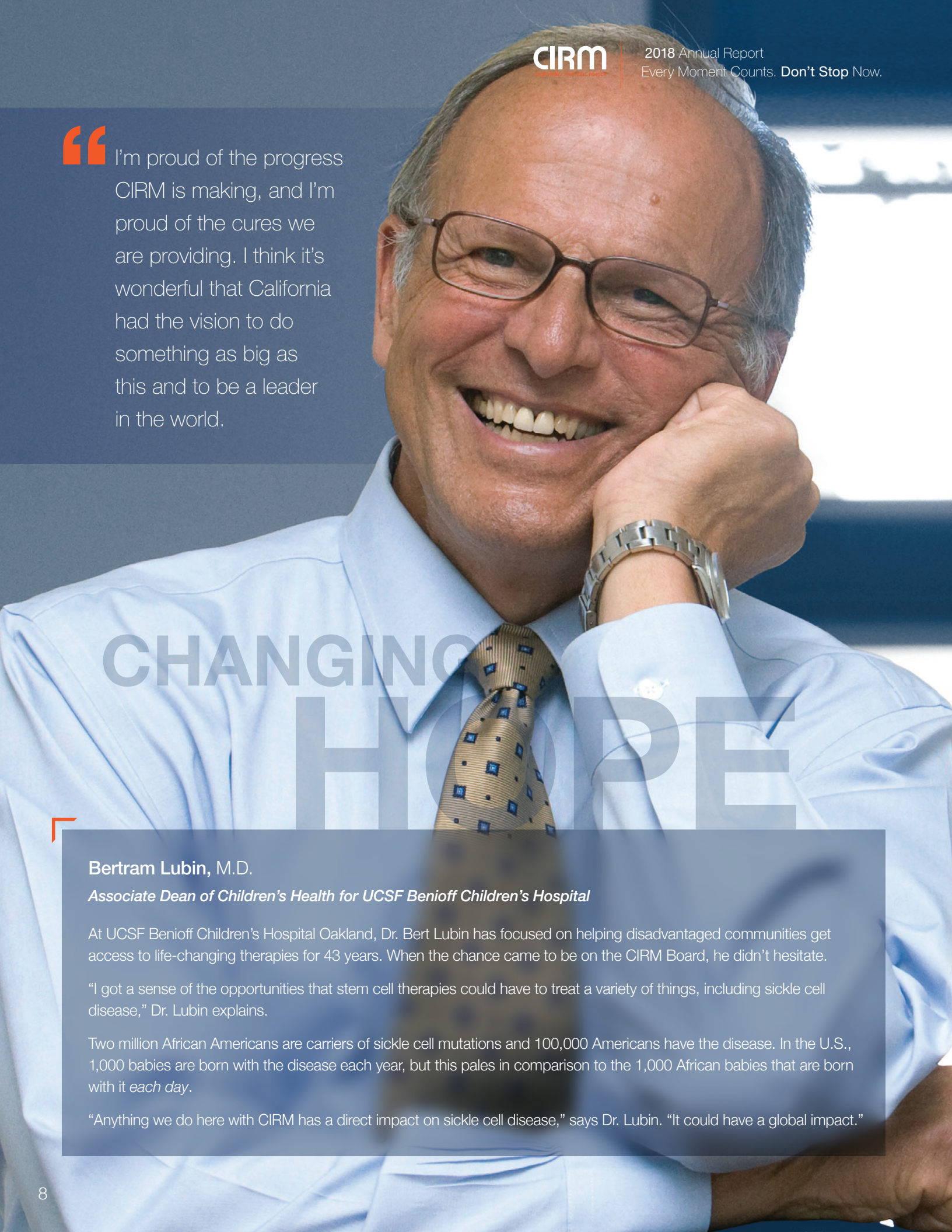
2016 | **$153 million**

2015 | **$40.5 million**

New Private Industry Investment by Year

Where they are. Right now.

In 2016, we celebrated Brenden Whittaker being the first person cured of X-CGD, a rare immune disorder that left him unable to fight off fungal or bacterial infections. Today, Brenden is on track to get his bachelor's degree in health sciences, the first step on the road to becoming a doctor. He says he remains as grateful as ever to UCLA's Don Kohn (see page 21) and CIRM for making this possible.



> "I'm proud of the progress CIRM is making, and I'm proud of the cures we are providing. I think it's wonderful that California had the vision to do something as big as this and to be a leader in the world.

CHANGING HOPE

Bertram Lubin, M.D.

Associate Dean of Children's Health for UCSF Benioff Children's Hospital

At UCSF Benioff Children's Hospital Oakland, Dr. Bert Lubin has focused on helping disadvantaged communities get access to life-changing therapies for 43 years. When the chance came to be on the CIRM Board, he didn't hesitate.

"I got a sense of the opportunities that stem cell therapies could have to treat a variety of things, including sickle cell disease," Dr. Lubin explains.

Two million African Americans are carriers of sickle cell mutations and 100,000 Americans have the disease. In the U.S., 1,000 babies are born with the disease each year, but this pales in comparison to the 1,000 African babies that are born with it *each day*.

"Anything we do here with CIRM has a direct impact on sickle cell disease," says Dr. Lubin. "It could have a global impact."

2018 Industry Support

Disease	Grantee	Investment/Industry Partner	2018 Funding
Kidney Failure	Humacyte, Inc.	Series C	$75 million
Multiple Myeloma	Poseida Therapeutics, Inc.	Series B	$31 million
Adenosine Deaminase-Deficient Severe Combined Immunodeficiency	Orchard Therapeutics	GlaxoSmithKline	Undisclosed
Acute Myeloid Leukemia	Nohla Therapeutics	Series B	$56 million
Acute Myeloid Leukemia and Advanced Colorectal Cancer	Forty Seven, Inc.	Initial Public Offering	$113 million
Kidney Failure	Humacyte, Inc.	Fresenius Medical Care	$150 million
Adenosine Deaminase-Deficient Severe Combined Immunodeficiency	Orchard Therapeutics	Series C	$150 million
X-Linked Severe Combined Immunodeficiency	Dr. Sorrentino (St. Jude's)	Mustang Bio	Undisclosed
Type 1 Diabetes	ViaCyte, Inc.	CRISPR Therapeutics	$25 million
Type 1 Diabetes	ViaCyte, Inc.	W.L. Gore & Associates, Inc.	$10 million
Advanced Solid Tumors	Fate Therapeutics	Follow-on Public Offering	$144 million
Adenosine Deaminase-Deficient Severe Combined Immunodeficiency	Orchard Therapeutics	Initial Public Offering	$226 million
Spinal Cord Injury	Asterias Biotherapeutics	BioTime, Inc.	Undisclosed
Type 1 Diabetes	ViaCyte, Inc.	Series D	$80 million

Where they are. Right now.

When retinitis pigmentosa left Rosie Barrero legally blind (as we reported in our 2016 Annual Report), she wondered if she would ever see the faces of her children again. After a CIRM-funded stem cell treatment, she did.

Today, she can see her children grow, blossom and succeed.

"One of my twins is in her second year of college," said Barrero. "I'm able to FaceTime with her and see what an amazing young adult she is becoming. Her twin brother with special needs is quite the handsome young man. And recently, my brilliant 16-year-old daughter and I made some beautiful floral arrangements—something you just can't do well with impaired vision."

Five-Year Goals

CIRM's operational performance

2018 was the third year of implementing CIRM's five-year strategic plan. This bold plan focuses on cutting in half the time it takes to get innovative scientific ideas through the stages of research. CIRM now has efficient and effective systems in place to bring in projects with the greatest potential for success. We are readily equipped to manage a world-class portfolio of clinical projects that offer as many chances as possible to treat and cure debilitating diseases, illnesses and injuries once considered incurable.

That approach is producing impressive results. We are reducing administrative costs per application and speeding up the time it takes to move those applications through our review process. All this is done with no sacrifice in quality.

OPERATIONAL ACHIEVEMENTS INCLUDE:

- Executing our five-year strategic plan, with many goals achieved ahead of schedule
- Increased the number of programs in clinical trials
- Strengthened relationships with investors and industry to support an active pipeline of private funding for CIRM-supported projects
- Lowered operating costs and increased efficiency, while also improving standards of performance
- Expedited grant funding, getting projects funded and off the ground faster

> At CIRM, our goal is to always improve, always get better, work smarter and faster

CIRM's 2020 Goals and Progress

BIG 6 2020

Introduce 50 new treatment candidates into development

Status **33** candidates

Increase projects advancing to the next stage of development by 50 percent

Status **110%** increase

Enact a new, more efficient regulatory paradigm for cell therapies

Status **5** CIRM-funded therapies fast-tracked by FDA via RMAT

Operational Highlights

CIRM Impact

3 Fewer weeks to agree on a contract

4 Years of "always open" clinical-stage funding

38 Partnership events (licenses, options and additional funding) to date

57 Progression events since 2016, marking CIRM's ability to advance projects to the clinical stage

70+ Clinical trials initiated through CIRM's Alpha Stem Cell Clinics Network

72 Clinical Advisory Panels convened (*an 80 percent increase since 2015*)

886 CIRM iPSC Repository lines sold to date *(350 in 2018)*

1,000 Stem cell projects funded since CIRM's inception

1,180 Patients in CIRM-supported clinical trials, past and present

LIVING OUR GOALS

Reduce translation time (discovery to clinical trial) by 50 percent

Status **4** candidates to IND within 18 months

Add 50 new clinical trials to the CIRM portfolio

Status **33** trials added in three years (50 total)

Pair 50 percent of unpartnered clinical projects with commercial partners

Status **59%** partnered

Operational Highlights

A new regulatory paradigm

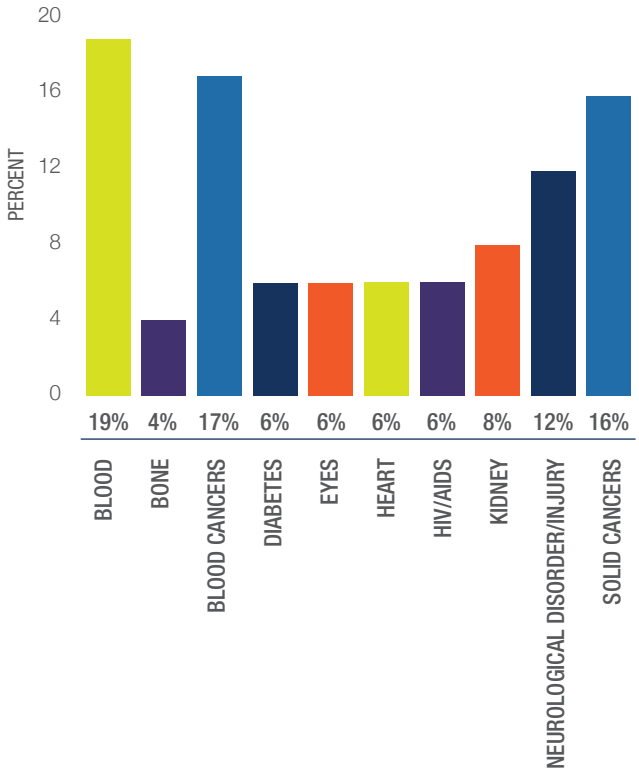
In 2015, we set some bold goals in our strategic plan, none more ambitious than creating an entirely new regulatory environment. But it is happening. In 2017, the FDA created the Regenerative Medicine Advanced Therapy (RMAT) designation to fast-track cellular therapies showing significant promise, giving them priority review status. Of the 25 RMAT programs to date, five are funded by CIRM.

CIRM has funded 1,000 projects at more than 70 institutions in California and is the largest single funder in the world of clinical research for stem cell and regenerative medicine. More than 2,700 medical discoveries have been peer reviewed and published in scientific journals. ***But, most importantly, lives have been saved, second chances have become possible and cures have risen beyond hope.***

> I learned that the reward of research is not the prestige of discovering the next groundbreaking cure, but rather the knowledge that perseverance in the face of obstacles could one day transform peoples' lives for the better.

Angelina Quint, participant in SPARK, the Summer Program to Accelerate Regenerative medicine Knowledge

Clinical trials funding by disease indication



> We are so grateful. CIRM has been a perfect partner in helping bring this approach, blending stem cell therapy and tissue engineering together. But it's the patients—*seeing them*—that keeps me motivated to do the science, to keep persevering.

RELENTLESS DRIVE

Diana L. Farmer, M.D.

Fetal and neonatal surgeon and chair of the Department of Surgery at UC Davis Health

Spina bifida, a birth defect where the spine does not form properly (often before a woman even knows she is pregnant), occurs in up to 2,000 children a year in the United States. The condition is the most common cause of lifelong paralysis and frequently leads to other serious health problems affecting the bowel and bladder. There is no cure.

Since 2008, University of California Davis physician Diana Farmer, an internationally renowned fetal and neonatal surgeon, has been working to help children with spina bifida walk. But now her sights are set on using stem cells transplanted into the fetus to correct the problem even before the baby is born. Dr. Farmer has successfully cured spina bifida in sheep and bulldogs as a proof of concept and, with CIRM's help, she is on the way to bringing this to human clinical trials.

Though still in the development stage, there may be a potential cure within our lifetime for a devastating condition that has plagued us for most of human history.

Operational Highlights

Establishing world-leading stem cell clinical trials for patients who need them the most

Alpha Stem Cell Clinics Network

Developing the most promising stem cell therapies is important, but without skilled teams to deliver those therapies to patients, the work is only half done. That's why we created the CIRM Alpha Stem Cell Clinics Network—six world-class medical facilities that have the expertise to deliver proven stem cell treatments and FDA-sanctioned clinical-trial therapies to patients.

Each year, the Alpha Stem Cell Clinics organize a CIRM-hosted statewide symposium, showcasing the work of each clinic and bringing together researchers, scientists, patients and their advocates, as well as the public, in a thoughtful discussion on stem cell therapies. The 2018 meeting at UCLA was successful and highlighted the power of a patient-centered approach.

The network has supported more than 70 clinical trials, targeting more than 40 different diseases and enrolling more than 400 patients to date.

CIRM
ALPHA CLINICS
Delivering Patient Treatments

40+ Disease Indications

70+ Clinical Trials

400+ Patients Enrolled

iPSC Repository

Human pluripotent stem cells are unique in that they can be grown in a lab and turned into any type of cell in the body. Because the genetics underlying human disease are complex, detailed genetic information about each stem cell line, as well as multiple lines that represent genetic variability between patients, is needed to make progress toward cures.

To address this need, CIRM created the world's largest induced pluripotent stem cell (iPSC) bank. iPSCs can be reprogrammed to have the same genetic makeup, including any disease-causing mutations, as the person from whom the original cells were taken. The CIRM iPSC Repository houses a collection of stem cells from thousands of individuals, some healthy, but others who have heart, lung, liver or other diseases or disorders.

The CIRM iPSC Repository was established to harness the power of iPSCs as tools for disease modeling and drug discovery. The Broad Institute's Stanley Center for Psychiatric Research and Harvard University are using the CIRM iPSC Repository to study disorders, such as autism. The Broad Institute has embarked on whole genome sequencing (WGS) of hundreds of lines from the CIRM repository with the aim of identifying the genes associated with neurological disorders and using this information as a starting point to find cures.

> The treatments being developed with CIRM support are so important. They offer a potential cure for a disease, and a community, that desperately needs one.

Marissa Cors

Diagnosed with sickle cell disease at 6 months old

Nearly 40 years after her diagnosis, Marissa Cors says living with sickle cell disease takes a toll, both physically and emotionally.

Cors says living with the disease means being in a constant state of pain and a constant state of limbo. She has no idea when the next crisis is going to come, how bad the pain will be or how long it will last.

"It means being hospitalized and having to put your life on hold so often that it's hard to have a job, hard to have a career or lead a normal life," she says. "It's hard to do the things everyone else takes for granted."

Where they are. Right now.

On the cover of our 2017 Annual Report, we featured Ronnie Kashyap, who was diagnosed with SCID (a rare life-threatening immune disorder) shortly after being born. A CIRM-funded clinical trial at UCSF helped restore Ronnie's immune system—and one year later—he's a healthy, thriving young boy able to do everything children do, including celebrating Diwali, the Hindu festival of lights, with his parents.

Operational Highlights

Advisory panels usher in real change, for real people

CIRM's approach to identifying and supporting significant science is unlike that of any other agency in the world. Our unique blend of public and private partnerships has created a completely new model for faster, more efficient and effective medical advancements.

Because of its role as a global hub for stem cell research, CIRM has become a valued source of knowledge, information, data, experience and expertise. As the field of stem cell therapies has evolved, CIRM remains at the center of it, helping shape the future, determined to bring the benefits of a new era of medicine home to California.

CIRM may be the hub of an industry, but patients and their advocates are at the heart of CIRM. They are involved at every stage of our process, hold 10 of 29 seats on CIRM's governing Board and serve on advisory panels that guide CIRM-supported clinical-stage projects.

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Right now.

Advisory panels provide support, guidance and patients' perspectives

When the CIRM governing Board approves a project, that is just the first step in our efforts to help it succeed. We have also created two unique, innovative groups to support the scientists every step of the way.

Clinical Advisory Panels

For every new clinical trial that we fund, we create a Clinical Advisory Panel (CAP) to support, guide and advise the researchers. A CAP consists of at least three advisors: a CIRM Science Officer, an independent stem cell expert and a patient advocate. They help the researchers plan the clinical trial, troubleshoot potential pitfalls and work collectively to overcome any problems along the way. The role of the patient advocate is particularly critical, because it ensures that the voice and the needs of the patient are front and center in designing the trial.

Translational Advisory Panels

A Translational Advisory Panel (TAP) is like a CAP, but designed to support an earlier stage of research, where scientists are conducting the studies needed to show that an approach holds promise for clinical applications. If a project succeeds at the translational stage, it takes a big step toward a clinical trial, where a therapy is tested on human subjects. Modeled after the successful CAP program, the first four TAPs were formed in 2018.

> I like to think that I am a bridge between patients and subjects, and the healthcare providers and scientists that they interact with.

ADVOCATING CHANGE

Gigi McMillan

Patient Advocate

"I have personal experience with life-threatening illness," says Gigi McMillan. "My own son had brain cancer when he was 5 years old."

McMillan is part of a new breed of patient advocates, people who want to ensure that the patient is part of the search for new therapies right from the start. She personifies the important role that patient advocates play at CIRM. She is on a Clinical Advisory Panel for a brain cancer clinical trial we fund. She is also an inspirational speaker who reminds all of us why we do this work.

"I know exactly how it feels to desire a cure with my whole being and be willing to take a chance on an experimental procedure that offers no guarantee," says McMillan. "My goal is to help all the stake-holders—patients, subjects, doctors, scientists—understand that ethical research depends on valid science and honest relationships."

Spotlight on change

Shining new light on neurodegenerative disorders

For as long as scientists have been studying stem cells, they have held out the hope that one day they could be used to treat diseases of the brain and central nervous system, such as Parkinson's disease and amyotrophic lateral sclerosis (known as ALS or Lou Gehrig's disease). Projects that CIRM is funding are bringing that day a lot closer and could help millions of people worldwide.

ALS

In the U.S., about 6,000 people are diagnosed with ALS each year. ALS usually strikes people between the ages of 40 and 70, who face an average survival time of just two to five years. People with the disease lose the ability to move their muscles. Over time, their muscles atrophy and they become paralyzed. Premature death is inevitable. There is no effective therapy for the disease.

Two CIRM-supported initiatives are underway to address ALS:

Researchers at **Cedars-Sinai Medical Center** in Los Angeles are running a CIRM-funded early-stage clinical trial using stem cells that have been turned into astrocytes, the brain cells that protect the cells destroyed by ALS. These astrocytes have been engineered to boost their protective ability in order to thwart the progression of the disease.

BrainStorm Cell Therapeutics has a Phase 3 clinical trial using cells taken from the patient's own bone marrow. These stem cells are then modified to boost their production of factors that are known to help support and protect neurons, the cells destroyed by the disease. Earlier-stage trials suggested this approach was safe and showed promise in slowing down the progression of the disease in some patients.

Parkinson's disease

Parkinson's disease affects approximately 1 million people in the U.S. and 7 million people around the world. It occurs when neurons, the nerve cells in the brain that control movement, die off.

CIRM is funding a team from **University of California San Francisco** and **Cedars-Sinai Medical Center**. The team is testing cells that are engineered to have higher quantities of a chemical that can protect vulnerable brain cells and slow down progression of the disease.

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> When I talk about CIRM, I tell people if you live in California you should be proud of how your money is being spent — and how it's making a difference in people's lives.

UNWAVERING RESOLVE

David Higgins, Ph.D.

CIRM Board member, patient advocate and patient

For David Higgins, Ph.D., Parkinson's disease is a family legacy. His maternal grandmother and uncle suffered from the disease and, in early 2014, his mother died with Lewy body dementia, which is related to Parkinson's disease. In his late 40s, Higgins began experiencing Parkinson's symptoms and in 2011 was diagnosed with the disease.

Higgins has become an advocate for people with Parkinson's and their caregivers. He is also determined to help find a cure and advocates for increased research funding. He uses his personal experiences to work to improve quality of life issues through education and support.

"I think what CIRM has done is critical," says Higgins. "They've created a new way of funding the best science in the world and enabled a way to involve the community in decision-making."

A Global Presence

Putting California's stem cell initiatives on the map

Increasingly, global organizations invite CIRM's experts to share their insights and experiences, a reflection of the increasing influence of CIRM on medical science around the world. It is our hope that the visibility of CIRM on a world stage will drive even greater investment into California's regenerative medicine ecosystem.

World Stem Cell Summit

At the World Stem Cell Summit in Miami, CIRM's president and CEO, Dr. Maria Millan, shared insights about the importance of the CIRM Alpha Stem Cell Clinics Network not only in delivering stem cell therapies to patients, but also in creating a new, more collaborative approach to medicine. As a team, CIRM covered topics ranging from public/private partnerships to regulatory considerations to the importance of state funding for advancing the field.

Facebook Live

Social media is an important aspect of our community outreach efforts, enabling us to engage far more people than we could in person. A new communications strategy introduced in 2018 was CIRM's "Ask the Stem Cell Team," a series of live discussions on Facebook featuring CIRM-funded researchers presenting highlights about their work and taking questions live from viewers. The sessions reached more than 19,000 people, with more than half of the audience viewing from outside California and as much as 10 percent of the audience from outside the U.S.

International Vatican Conference: Unite to Cure

Dr. Maria Millan, a panelist at the 2018 Unite to Cure Conference at the Vatican.

In April, at the International Vatican Conference: Unite to Cure, speakers and experts from every region around the globe came together to address how science, technology and 21st century medicine will impact culture and society. CIRM's Dr. Maria Millan participated on a panel discussing "Public/Private Partnerships to Accelerate Discoveries," where she highlighted the unique acceleration approach pioneered by CIRM.

"I found the science incredible. You could eliminate an otherwise fatal disease, correcting the gene defect in the bone marrow stem cells and letting nature do the rest to build a new immune system. It was amazing. It still is.

DELIVERING CURES

Donald B. Kohn, M.D.

Researcher and Professor, University of California Los Angeles, Department of Microbiology, Immunology and Molecular Genetics

Early on in his medical career, Dr. Don Kohn made a promise to himself to pursue stem cell research that could treat life-threatening diseases.

Therapies that came about as a direct result of Dr. Kohn's work have treated more than 40 children who had the life-threatening disease ADA-SCID (an immune deficiency). Many of these children are now living normal, healthy lives. Dr. Kohn has also gone on to create clinical trials for sickle cell disease and X-linked chronic granulomatous disease, or X-CGD. *(See Brenden Whittaker's story on page 7.)*

"CIRM funding has been essential to the overall success of my work," says Dr. Kohn, "supporting me in navigating the complex regulatory steps of drug development, including interactions with the FDA and toxicology studies that enhanced and helped drive the ADA-SCID clinical trial."

2018 CIRM Game Ball Winners

People driving performance

People think of CIRM as a funding agency, but our people are one of our most precious resources. We honor those who regularly go beyond the call of duty to help patients in need. We recognize these individuals with Game Balls.

Lila Collins, Ph.D.

Associate Director, Therapeutics

Dr. Collins is a Science Officer at CIRM who works closely with investigators to recruit and manage candidates for clinical-stage awards. She made her mark at CIRM—and in the field of regenerative medicine—by stepping out of her comfort zone and going above and beyond to accelerate projects despite twists, turns and major challenges.

Tricia Chavira

Project Manager, Review

Day to day, Tricia manages the process that ushers in the most promising grant applications through CIRM to independent expert review panels and then on to our Board. For organizing three review meetings (two of them in person) in 30 days and for compressing a typical two-day meeting into a single day, she receives a 2018 Game Ball.

Todd Dubnicoff, Ph.D., **Kevin McCormack, Maria Bonneville, Karen Ring**, Ph.D.

Doug Guillen

Senior Executive Assistant to the Vice Chair

In his time at CIRM, Doug has worn many hats. He started off as the office manager in the information technology department, then moved into an executive assistant role and is currently a project manager for a variety of initiatives. He wins a Game Ball for stepping up to the plate and being versatile, flexible and responsive.

Eliana Barnett

Senior Executive Assistant to the President and CEO

Eliana is the quintessential organizer, keeping projects and people running on schedule and in the right direction. Her detail-mindedness and can-do attitude supporting CIRM's president and CEO, chairman of the Board and the Business Development and Fund-raising teams are recognized with a 2018 Game Ball.

Kelly Shepard, Ph.D.

Associate Director, Discovery, Translation and Education

A Science Officer who oversees Discovery and Translation research programs at CIRM, Dr. Shepard helps investigators begin the transition of taking stem cell therapies from a researcher's bench to a patient's bedside. She is awarded a Game Ball for creating and maintaining CIRM's interactive Active Awards Portfolio Dashboard.

Communication Team

Maria Bonneville, Todd Dubnicoff, Kevin McCormack and Karen Ring,

This team effectively communicates CIRM's accomplishments and progress to the public through CIRM's blog (The Stem Cellar), social media and traditional media outlets. They translate complex science into everyday English, chronicling scientific history in real time.

Financial Review

2018 Financial Reconciliation

	January 1, 2018	December 31, 2018
Committed Balance	$2.48 billion	$2.6 billion
Uncommitted Balance	$269 million	$144 million
Balance Under Active Management	$435 million	$351 million
Number of Programs Under Active Management	263	214

2019 Approved Budget

Approved budget for 2019 calendar year

Program	Investment
Education	$0.6 million
Discovery	$0.0 million
Translation	$20.0 million
Clinical	$123.0 million
Total	**$143.6 million**

> “Today, thanks to the 7.2 million voters who authorized the California Institute for Regenerative Medicine, or CIRM, we have something better than hope; we have results, accomplishments, people made well — and a systematic way to fight chronic disease.
>
> **Don Reed,** Vice President of Public Policy at Americans for Cures

Community

Our commitment to our community

At CIRM, we know that great science takes time. That's why we are investing in the future, educating the next generation of stem cell scientists. We owe it to the people of California to let them know how we are investing their money, so we regularly take to the road to deliver that message in person.

High School Students

For many of us at CIRM, one of the highlights of the year is SPARK, also known as the Summer Program to Accelerate Regenerative medicine Knowledge. This gives high school students a chance to spend their summer vacation working in a world-class stem cell research lab. The students reflect California's diverse population and include many who may not normally be able to take part in research internships because of financial considerations. The sheer joy and enthusiasm the students bring to this work are a powerful reminder of just how exciting this research is.

Undergraduate and Master's Students

CIRM's Bridges to Stem Cell Research Awards program was created to help train the next generation of stem cell scientists in California. Since we launched Bridges, almost 10 years ago, more than 1,200 students have taken part in the program. Half of these past Bridges trainees are currently working in full-time jobs at research institutions or companies, and almost one-third have enrolled in graduate or professional school programs.

Patient Advocate Events

In 2018, CIRM held its first patient advocate event at the University of California, Riverside. It was a chance to talk to both the public and the scientific community about the work we are doing and to hear from them about their hopes and plans.

50 Clinical Trials funded

CIRM has funded 50 clinical trials in 34 different disease types, including early-stage trials that show promise for addressing some of today's most challenging diseases, conditions and injuries for which there are no known cures.

- Age-related Macular Degeneration
- Alpha Thalassemia Major
- Amyotrophic Lateral Sclerosis
- B Cell Cancers
- Beta Thalassemia
- Blood Cancer
- Bone Marrow Transplant and Viral Infection
- Brain Cancer
- Colon Cancer
- Heart Disease associated with Duchenne Muscular Dystrophy
- Heart Failure
- HIV/AIDS
- HIV-related Lymphoma
- Huntington's Disease
- Kidney Failure
- Leukemia
- Leukemia, Acute Myeloid (AML)
- Lung Cancer
- Melanoma
- Multiple Myeloma
- Osteoarthritis
- Osteonecrosis
- Pulmonary Hypertension
- Retinitis Pigmentosa
- Severe Combined Immunodeficiency, Adenosine deaminase-deficient (ADA-SCID)
- Severe Combined Immunodeficiency, Artemis deficient (ART-SCID)
- Severe Combined Immunodeficiency, X-linked (X-SCID)
- Sickle Cell Disease
- Skin Cancer
- Solid Tumors
- Spinal Cord Injury
- Stroke
- Type 1 Diabetes
- X-linked Chronic Granulomatous Disease

Where they are. Right now.

In 2011, Rich Lajara suffered a serious spinal cord injury. Soon after, in a groundbreaking clinical trial, surgeons transplanted stem cells into his spine to determine if the cells could repair the damage. He was the first patient treated in a CIRM-funded clinical trial. Patients who were later enrolled in a follow-up trial have made encouraging progress, regaining sensation and the use of their arms and hands.

Lajara knows that finding treatments for a condition that previously had no hope takes time. Though still using a wheelchair, he believes that his involvement helps advance the science, and that each person who takes part in a clinical trial takes us one step closer to a treatment. That's why he's supporting CIRM's work and fighting for something better than hope.

"In my heart, I believe that being in a wheelchair is temporary. In my lifetime, I'm going to walk. So, it helps knowing there's something over the horizon, some level of a cure.

CIRM
CALIFORNIA'S STEM CELL AGENCY

California's Stem Cell Agency
Lake Merritt Plaza, 1999 Harrison Street, Oakland, CA 94612

www.CIRM.ca.gov