



Letter to the People of California

Seven million Californians voted for Proposition 71 — the California Stem Cell Research and Cures Initiative — in November of 2004. The measure establishes the California Institute for Regenerative Medicine (“CIRM” or the “Institute”), a new state agency, and authorizes the allocation of \$3 billion in public bond funds for scientific and medical research in California. The Institute has a clear and simple mission: to support stem cell research and other vital medical technologies to develop therapies and potentially cures for patients suffering with chronic disease and injury.

Californians believe that stem cell biology has the potential to prevent, diagnose, treat, and cure disease and disability, backing that belief with a multi-year commitment matched by no other state or country. Since its first meeting in December 2004, the CIRM governing board — the Independent Citizens Oversight Committee (“ICOC”) — and staff have been working tirelessly to fulfill the voters’ mandate.

The ICOC, a distinguished 29-member body appointed by a group of California’s elected officials and public university chancellors, includes patient advocates, members of the private sector, and the leadership of some of the state’s top research institutions. The ICOC members, must approve all grants and loans, regulations, standards, and policies in public session conducted under the Bagley-Keene Open Meeting Act. The ICOC elected its Chairman, Robert N. Klein, and Vice Chairman, Edward E. Penhoet, Ph.D.; appointed Zach W. Hall, Ph.D., President and Chief Scientific Officer of CIRM; and named key scientific and administrative personnel.

Following the blueprint provided by the California Stem Cell Research and Cures Act (the “Act”), the ICOC appointed working groups and subcommittees that developed medical and ethical standards for research with the assistance of the National Academies, along with critical governance, administrative, and regulatory policies to ensure that CIRM’s efforts meet the highest standards of public integrity and accountability. These policies are crafted in public under the ultimate auspices of the ICOC—but it is the collaboration among the working groups, CIRM staff, elected officials, patients, and members of the public that has laid the foundation for a large-scale, vigorous stem cell research program. The challenge for the Institute’s first eighteen months was daunting: 1) initiate a bold, new

scientific venture at the frontier of biomedical research; 2) establish the regulatory and administrative framework to support hundreds of research grants; and 3) build a new state agency to carry out these functions. Our achievements for the year are substantial in each of these areas. They are summarized on the following pages and in the body of the annual report.

CIRM Initiatives Laid the Foundation for Strong Science

CIRM has worked hard in this first eighteen months of existence to ensure that the foundation for its stem cell research funding program is in place. Among our key accomplishments:

- CIRM solicited and received Research Fellowship applications for the CIRM Training Program in Stem Cell Research to train pre-doctoral, post-doctoral and clinical fellows, and to build collaborations across research areas to create a new generation of interdisciplinary stem cell scientists in California. The Scientific and Medical Research Funding Working Group reviewed the proposals and rated them based upon scientific merit, and the ICOC completed a final review and approval of grants to 16 outstanding California research institutions to train 169 brilliant young stem cell scientists and clinicians. The awards for the first year grants were made possible on April 6, 2006 through the leadership of six philanthropic individuals and foundations who purchased Bond Anticipation Notes of the State of California, despite the ongoing litigation challenging the state's ability to repay those notes.
- The ICOC appointed the members of the Scientific

and Medical Accountability Standards Working Group, composed of five ICOC patient advocates, nine nationally-recognized scientists, and four biomedical ethicists, to develop ethical standards governing CIRM-funded research. (Membership of the Working Group, including the ICOC Members, is on page 28.)

- The ICOC appointed members of the Scientific and Medical Research Funding Working Group, including fifteen nationally prominent stem cell scientists from outside of California, as well as seven patient advocates from the ICOC, to develop criteria for reviewing scientific applications and to evaluate research proposals. (Membership of the Working Group, including the ICOC Members, is on page 27.)
- The ICOC appointed a Scientific and Medical Research Facilities Working Group that is responsible for overseeing the development of research facilities by the Institute. (Membership of the Working Group, including the ICOC Members, is on page 26.)
- CIRM appointed a nationally prominent scientific administrator, Arlene Chiu, Ph.D., as Director of Scientific Activities.
- CIRM organized a major scientific conference, *Stem Cell Research: Charting New Directions for California*, which brought biomedical experts from all over the world to advise CIRM on scientific priorities for funding.
- CIRM accepted an invitation to join the Interna-

tional Stem Cell Forum, a prestigious multinational organization of scientific funding agencies representing 17 countries that facilitates worldwide collaboration in stem cell research

Regulatory and Administrative Infrastructure Protects Science

CIRM has been a national leader in setting the highest medical and ethical guidelines and in developing grant administration and intellectual property policies. Among our top achievements:

- Many ICOC appointees participated in a public meeting in December 2004, organized by the Board on Life Sciences of the National Research Council of the National Academies, where national experts in scientific administration contributed to a broad platform of information on “best practice” policy alternatives for key ethical, regulatory and administrative policies.
- The ICOC approved draft regulations for medical and ethical standards modeled after the National Academies’ *Guidelines for Human Embryonic Stem Cell Research*. The interim CIRM standards are the first comprehensive state regulations in the country for stem cell research.
- The ICOC approved an Intellectual Property Policy for Non-Profit Institutions that surpasses national standards and Federal statutes. The policy requires the prompt sharing of research results, provides a financial return to the State for intellectual property (beyond the most important potential return: new therapies), and ensures accessibility to treatments for low-income and uninsured Californians.

- CIRM developed, and the ICOC approved a grants administration policy that establishes processes and procedures for all CIRM-funded research at non-profit California institutions.

Building a State Agency from the Ground Up

Immediately after passage in November, 2004, CIRM began building itself into California’s newest government agency.

- After a vigorous competition between 10 California cities, the ICOC selected San Francisco for its headquarters, based on the city’s proposal that provided \$18 million in donated benefits and services to CIRM, including:
 - 20,000 square feet of office space, rent free for a decade;
 - 16,000 hotel rooms over 10 years (2,000 free rooms with the balance discounted);
 - Seven conference venues of 300-50,000 seats free for 10 years.
- The San Francisco proposal saves taxpayers money and allows the Institute to devote more funds to scientific research. This represents the first time in the history of the state that a public/private partnership group has come together to financially underwrite a main headquarters facility and incentive package for a California government agency.
- The ICOC established conflict-of-interest policies for the ICOC, CIRM employees, and working group members that go beyond state law.

- The ICOC established open meeting policies and held more than 70 public meetings (as of June 2006) at sites throughout California.
- CIRM and the ICOC developed an organizational structure for CIRM and established personnel compensation policies.

Funding the Agency Grants: Financial Innovation and Civic Support

Although groups opposed to stem cell research sought to prove, through litigation, that they could stop the State of California from implementing the grant program, the CIRM successfully funded its first 169 research fellows grants in April, 2006. This represented the beginning step in authorizing an innovative interim financing program to carry the CIRM grant program through the litigation period. The steps to that process are outlined below.

CIRM received authorization from the State’s independent Finance Committee to sell up to \$200 million in bond anticipation notes (BANs), as interim funding for CIRM operations and grants. The first \$14 million in BANs were sold on April 4, 2006, to the following California philanthropic foundations:

Beneficus Foundation	\$2 million
Blum Capital Partners LP	\$1 million
William K. Bowes Foundation	\$2 million
The Broad Foundation	\$2 million
Jacobs Family Trust	\$5 million
The Moores Foundation	\$2 million

The second \$31 million in second round BANs, closed in

November of 2006 are as follows:

Mr. J. Taylor Crandall	\$1 million
Gordon and Betty Moore Foundation	\$10 million
Dr. Gordon E. Moore Jewish Community Endowment Fund	\$5 million
H&S Investments I, LP	\$1 million
Seventh Street Warehouse Partnership	\$2 million
Steven L. Swig and Mary Green Swig	\$1 million
The David and Lucile Packard Foundation	\$5 million
The Sandler Family Supporting Foundation	\$5 million

Several key donors whose charitable contributions have empowered a substantial portion of our work should also be acknowledged. The agency’s efforts to lead the country in developing medical, ethical, and conflict of interest standards, and to process its first grants were largely funded by a generous contribution from Ray and Dagmar Dolby and their family foundation. And important supporting contributions for scientific meetings and strategic planning activities were made possible by a gift from the Richard and Rhoda Goldman Fund.

Pursuing the Voters’ Mandate

Litigation challenging the constitutionality of the California Stem Cell Research and Cures Act (Proposition 71) currently precludes the State from issuing the authorized general obligation bonds to fund stem cell research at acceptable interest rates. The Attorney General, Bill Lockyer, has strongly and successfully defended

the constitutional merit of Proposition 71. On April 21, 2006, Judge Bonnie Lewman Sabraw of the Alameda County Superior Court delivered a ruling that found the California Stem Cell Research and Cures Act constitutional in its entirety.

Judge Sabraw found that the CIRM was firmly under the management and control of the state, stating in part:

The evidence at trial establishes that the application of the Act has been in compliance with its statutory framework, and that CIRM and the ICOC are operating in the same fashion as other state agencies. Each ICOC member, and each alternate, has taken the oath of office and publicly filed Form 700, the standard form California public officials file to disclose financial holdings. The ICOC developed and adopted incompatible activities statements, the conflict of interest code required by the Political Reform Act, and conflict of interest policies for ICOC members, CIRM staff, and members of each of the ICOC advisory groups. Between January 2005 and the date of the trial, the ICOC and its subcommittees, and its working groups held over 40 noticed, public meetings, in cities across the state, held pursuant to the Bagley-Keene Open Meeting Act. CIRM has responded to numerous Public Records Act requests.

Judge Sabraw also found that the Institute has been accountable to the public and has conformed to all state oversight requirements in carrying out its operations. The court's decision is a significant step forward toward the point in time when General Obligation bonds can be issued at reasonable interest rates to fund voter-mandated stem cell research. It is therefore a major victory for the CIRM to have assembled its substantial interim grant funding program for the next fiscal year.

The Superior Court decision has since been appealed, and a final conclusion is not expected until 2007, when we believe the voters' intentions will be upheld. Fifteen

AMICUS PARTIES

The following research institutions, hospitals, universities, and patient advocacy organizations filed an amicus brief in support of CIRM on October 12, 2005.

Patient Advocacy Groups

- Alliance for Aging Research
- Alliance for Stem Cell Research
- ALS Association
- Alzheimer's Association, CA Council
- Cancer Research and Prevention Foundation
- Christopher Reeve Foundation
- Cystic Fibrosis Research, Inc.
- Elizabeth Glaser Pediatric AIDS Foundation
- Juvenile Diabetes Research Foundation (JDRF)
- The Leukemia and Lymphoma Society
- Michael J. Fox Foundation for Parkinson's Research
- National Brain Tumor Foundation
- National Multiple Sclerosis Society
- Parkinson's Action Network
- San Francisco AIDS Foundation

Universities

- California Institute of Technology
- Keck Graduate Institute
- Stanford University
- University of Southern California

Hospitals & Institutes

- Cedars-Sinai Medical Center
- Children's Hospital & Research Center at Oakland
- Children's Hospital Los Angeles
- City of Hope
- Salk Institute of Biological Studies
- The Burnham Institute

Others

- Paul Berg, Nobel Laureate
- Southern California Biomedical Council

INNOVATION GRANTS

The ICOC approved three research initiatives that rely on \$31 million of bond anticipation notes and a \$150 million loan from the California Department of Finance.

Comprehensive Research Grants

(up to \$80 million over 4 years)

- Record of accomplishment in hESC research or closely-related field
- Opportunity to expand research or take promising new directions based on current research
Must be related to long-term therapeutic goal
- Topics include, but are not limited to:
 - Self-renewal and differentiation of hESCs
 - Derivation of new hESC lines, including disease-specific lines
 - Study of hESC-derived cells in animal models
 - Assessing tumorigenicity of hESCs and cells derived from them
 - Reprogramming of adult human somatic nuclei
 - Studies related to identification, storage, maintenance, stability and storage of hESCs

Seed Grants

(up to \$24 million over 2 years)

- Emphasis on new ideas, new investigators in the field
- No prior record of hESC research required
- No “preliminary data” required
- Criteria will emphasize innovation

Shared Research Laboratory Grants

(up to \$47.5 million over three years)

- Dedicated laboratory for culture of hESCs, including cell lines that are outside the federal guidelines
- Will support core equipment and trained personnel
- Services available for scientists from nearby institutions without facilities
- At up to five institutions, extra funds will be provided for formal course instruction, given several times per year for California scientists and trainees.

national patient advocacy organizations and fifteen of California’s most prestigious research institutions and universities (shown on the previous page) joined the litigation, in support of Proposition 71, in an amicus curiae brief. The courageous backing of those support groups provided a clear message to California’s court decision on the urgent need to expedite this litigation. It is our hope that our litigation will finally be resolved by the middle of 2007, at the State Supreme Court.

State of California Funding Breakthroughs

For the coming year, we are actively preparing for the availability of full public funding of more than \$300 million in General Obligation Bonds, so that we can quickly issue additional training, research, and facilities grants without further delay. In a bold and decisive move this past July, Governor Arnold Schwarzenegger directed the California Department of Finance to make a \$150 million loan to the Institute. This loan was authorized by Section 125291.60 of Proposition 71 and will help ensure California retains its national leadership in stem cell research, while the litigation is concluded. The loan funds are expected to be available in November of 2006, and they will allow CIRM to advance a major program of research in California for the benefit of patients worldwide. The ICOC has approved three major research initiatives that rely on the \$31 million of additional BAN’s funds and the \$150 million loan. Those programs are outlined at left..

The successes of our inaugural eighteen months, as well as those we will record going forward, are the cumulative efforts of many people, here in California, across the country, and around the globe. We are grateful to the residents and public interest groups who helped shape our scientific and governance policies; the experts who

helped navigate complex ethical and intellectual issues and chart the direction of our research funding; the elected officials who contributed advice and counsel to navigate the challenges of creating a new government agency; the CIRM staff who continually exceed high expectations; and finally, to the ICOC board members — their tireless dedication to our mission and the tremendous scope of their expertise is a great gift to all Californians.

A Focus on Therapies and Cures

Our overall organizational mission is to support and advance stem cell research and regenerative medicine under the highest ethical and medical standards for the discovery and development of cures, therapies, diagnostics and research technologies to relieve human suffering from chronic disease and injury. One of the ways in which we remain connected to our primary constituency, patients, is through a presentation series called "Spotlight on Disease." In cooperation with the non-profit organization, Alliance for Stem Cell Research, we have organized presentations before most ICOC meetings so that ICOC Members, CIRM staff, and members of the public are able to learn more about the state of stem cell science and the experience of patients within a particular chronic disease or injury.

One-page summaries of these very moving Spotlight presentations appear in the following pages: immediately after this introductory letter and at the end of the Annual Report itself. We hope you that in perusing these summaries, you capture a sense of the primary motivation for why we are working so hard every day to ensure that we meet our mission.

We are at a pivotal point in the history of medical

research. In approving Proposition 71 on November 2, 2004, the citizens of California created the vision of a future for humanity that holds the potential for remarkable progress in the understanding and treatment of chronic disease and injury.



Robert N. Klein, II
Chairman, Independent Citizens Oversight Committee