

To the people of California

A Message from the chair
ROBERT N. KLEIN

With \$1.15 billion in stem cell **research facilities** and faculty recruitments committed, global collaborations set, human trials underway and President Obama in the Whitehouse, the stem cell world changed in 2008.

Yet, for the California Institute for Regenerative Medicine (CIRM), the real change began November 2, 2004. The dynamic evolution of 2008 arose out of the will of 7,000,000 Californians voting in another year of financial crisis, to pass Proposition 71: a Constitutional Amendment and an Initiative, passed as one integrated ballot measure, creating a stem cell funding agency with \$3 billion in bond authority.

HOW FAR HAVE WE COME? In 2004 we needed to place these words in the California Constitution to assure the long-term freedom of scientific research to develop medical therapies:

“There is hereby established a right to conduct stem cell research involving adult stem cells, cord blood stem cells pluripotent stem cells and/or progenitor cells.”

In 2008, University of California, San Diego Assistant Professor Catriona Jamieson, because of this freedom and stable funding, commenced the first human trial of a therapy derived in part from Proposition 71-funded stem cell research: a therapy that may treat a myeloproliferative blood disease that can lead to leukemia and strokes. As 2009 commenced, less than a week after President Obama’s inauguration, the FDA approved stem cell therapy trials for acute paralysis—a therapy derived from embryonic stem cell research that originated in the laboratory of Hans Kierstead at the Reeve-Irvine Research Center at the University of California, Irvine.

With the new President and the beginning of the FDA trials, the stem cell revolution has now been truly launched. Yet, there is much more to do. In 2009, the new Congress and President will need to remove restrictions on federal funding for research with all human embryonic stem cell lines and for the creation of much-needed new embryonic stem cell lines. The International Society for Stem Cell Research (www.isscr.org) has posted a policy paper in the news archives reaffirming that embryonic stem cell research remains “the gold standard,” signed by a significant number of CIRM grantees. Yet, the Congressional battle to provide federal funding for the full range of stem cell research still lies before us.

FEDERAL FUNDING IS NOT SECURE In 1998 President Clinton tried to initiate embryonic stem cell research funding only to find in 1999 that the conservative resurgence of the House of Representatives forced him to abandon this commitment.

Proposition 71 and its constitutional protections for the full scope of stem cell research and its long term funding through 2018 will remain a safe harbor in a sea of change. California must sustain this revolution through early human trials if the stem cell revolution is to thrive through this volatile period.

We celebrate 2008 and the progress, but remain vigilant, focused on the mission, and cautiously optimistic, as the speed of scientific and clinical advances in stem cell research provide extraordinary breakthroughs and discoveries.

As we start 2009, we can also celebrate a major increase in NIH research funding for 24 months. At month 25, what happens? Can the nation sustain this research funding surge? We hope it can; but, we know California’s funding level will be sustained for more than 108 months. The funding stability must be there to carry these critical new therapies through early human trials, for which NIH has drastically reduced its funding.

FOCUS ON EARLY PHASE TRIALS The current financial crisis aggravates the recent, historical lack of capital in the developmental space between clinical studies and phase 2 human trials. It deepens and widens the “Valley of Death” that new stem cell therapies must navigate. Traditionally, NIH funding has not focused on this area, but Proposition 71 funding focuses on it as a mission critical core program objective. Both the basic research and the clinical trial ends of the research pipeline represent critical contributions to advancing stem cell therapies. Hopefully, the NIH will expand funding in this area or develop collaborative funding with CIRM for therapy development.

CIRM, in 2009, has already shifted its focus to funding this development resource gap. Announced CIRM programs include substantial funding for biotech companies, alone or in collaboration with academic institutions. In 2009 alone, \$60 million is scheduled for Translational Research grants, and \$210 million is scheduled for Disease Team grants and loans. In 2009, the Board will address resource allocations, in its strategic plan review, for early human clinical trials.

If efficacy can be proven, the public’s will cannot be reversed or defeated.

**By 2010,
a recent
economic study
suggests the
agency’s
funding will
have generated
at least
\$100 million
of new tax
revenue for
the State.**



We must sustain the translational element of this scientific revolution until two things happen:

- The value to patients is effectively proven with successful human trials of stem cell-based therapies.
- A path to affordable access to these stem cell therapies has been built for Californians and the world.

This will be California’s contribution in collaboration with great scientists and clinicians from many states and countries, and now the NIH. Certainly California has not and will not succeed in isolation.

California’s research has advanced with the inspired contributions of its peer review panels – drawn primarily from Europe and North America, all from outside of California. A list of the extraordinary men and women who have contributed their time to driving the scientific excellence of these peer review sessions is included on page 37 of this report. The patients and citizens of California are grateful for the dedication of these scientists and the special efforts of the Scientific and Medical Grants Working Group Chairs Stuart Orkin, Ali Brivanlou, John Sladek, Dennis Steindler and Rainer Storb; and Vice-Chairs Joan Samuelson and Jeff Sheehy.

CALIFORNIA’S RESEARCH ASSETS Entering 2009, CIRM will have approved funding more than \$500 million in scientific grants, with another \$300 million authorized in the grant and loan pipeline. Another \$1.15 billion has been authorized for the construction of new stem cell research facilities and faculty hiring (including \$880 million in donor and institutional matching funds). These facilities are scheduled for completion in 2010. With the Chairman’s Office, the Facilities Working Group that drove the Major Facilities competition was chaired by David Lichtenger, with board member David Serrano Sewell as the Vice-Chair.

Global collaborations with nations are in place, providing \$5 million from Australia for Early Translational grants and over \$50 million of international research funding from the United Kingdom, Canada, and Spain on the Disease Team Initiative RFA. These research funding contributions, covering the research conducted outside California, brings the total matching donor, international, and institutional funding commitments to over \$1 billion, on the first \$1 billion (by September 2009) in CIRM’s projected funding commitments. There is a moral imperative that we marshal every possible resource to match the vision of California’s voters. To date, the matching fund commitments have been remarkable.

EXTENDING THE FUNDING HORIZON The Initiative that created CIRM begins by establishing in the California Constitution, “The California Institute of Regenerative Medicine...to make grants and loans.” Beyond the classic grant programs, a loan program was envisioned for later stage research. The \$3 billion for research funding is not enough, unless substantial portions of the funding are recycled to push sufficient medical research through early trials to reach the broad scale momentum necessary to create an entire new field of medical therapies.

With the Chairman’s Office, the Loan Task Force, under the leadership of board member Duane Roth and Finance Subcommittee Chairman Michael Goldberg, guided the development of a loan program in 2008. The ultimate goal is to expand a \$500 million CIRM loan program with the hoped for proposed federal guarantees to yield a \$1 billion initial program. That amount would be scaled up by recycling an additional \$1 billion in repayment proceeds over the first decade of the program. In short, with \$500 million in federal long-term guarantees and recycled principal repayments, interest and stock warrant revenue from borrowers, over \$1.5 billion in additional resources could be added to the Proposition 71 research portfolio.

This loan program will provide funds to companies developing new cures for Californians and the world while also creating an ongoing source of funding for these critical commercial ventures.

When making critical funding allocations for research on mitigating or curing forms of cancer, heart disease, diabetes, dementia, arthritis, blindness, and stroke, among many candidate therapies, it is essential to our goals to expand our portfolio size through innovations – like the loan program. As we diversify the portfolio, our opportunities for success in the development of vital knowledge on the development path of chronic disease and the chance to prove successful therapies could be enhanced dramatically.

CALIFORNIA’S POLITICAL LEADERS ARE KEY The stem cell agency’s remarkable progress has, each year, been lifted and advanced by the special dedication of California’s constitutional and legislative leadership to the mission of developing stem cell therapies to reduce human suffering. For 2008, I would like to express the Board’s appreciation for their special contributions which has been recognized in detail on our Web site at www.cirm.ca.gov.

California is a state united behind the stem cell research mission. The first human therapy trials underway may take years to perfect, before patients can routinely benefit

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by the time the state’s general fund will pay the first \$15 million in debt service on the stem cell bonds. In addition, an estimated 13,727 job years will have been created by the major facilities funding alone. By 2010, just the new research facilities funded by CIRM and donors will also house over 2,200 scientists, clinicians and their research personnel. The long-term economic multiplier effects of this vast expansion in California’s biomedical research sector will launch a major wave of expansion in California’s second largest technology job sector – biotech.

THE ULTIMATE REWARD Beyond economic benefits, including potential relief from chronic health care costs for California’s patient families, government and businesses, the ultimate benefits we reach towards everyday are for each child, husband, wife or parent who is a patient. Last summer, I attended a Foundation Fighting Blindness event. A father, suffering from retinitis pigmentosa, a form of blindness, showed me his bionic eye that permitted him to see only bright lights and shapes. He said he was saving his other eye for stem cell therapies. His daughter stood by his side, only in her 40s, her eyesight deteriorating. She knew the future – blindness, or just possibly, stem cell therapies to repair and restore her sight and her father’s.

Will the pending collaboration of California scientists with the United Kingdom’s scientists on retinal disease accelerate human therapies? Large animal trials are already showing success in England. California scientists work in global collaborations; the world awaits the outcome. A father and a daughter await the outcome. Hope for California, hope for the world’s families is betting on the vision of 7,000,000 California voters. I am hoping for the day I can look this father and daughter in their eyes and they can see me.

Thank you California.

from this revolutionary field of medical science. That day will come in large part due to the commitment California has made – through its government sector (\$3 billion) and its civic sector (\$1 billion to date) – to drive this frontier forward for the benefit of mankind with treatments on the horizon for diabetes, heart disease, blindness, neurodegenerative diseases, forms of deafness and other chronic diseases.

By 2010, a recent economic study suggests the agency’s funding will have generated at least \$100 million of new tax revenue for the State,