To the People of California

A MESSAGE FROM THE CHAIR: ROBERT N. KLEIN, J.D.

For families suffering from chronic disease or injury, Proposition 71 has brought hope; for medical scientists who have dedicated their lives to reducing human suffering, it has been an inspiration; and for patient organizations, it created a paradigm change in the structure, scope and term of medical research funding in America.

To date, almost $260 million in grants have been approved by the governing board after a competitive, scientific peer review process, and another $300 million is in the approval process. All elements of the court system in California, including the Supreme Court, have exhaustively reviewed the grant making system, the medical and ethical standards, the conflicts policies and the constitutional authority of the governing board and the agency. The Supreme Court has found that all of the Initiative's aspects are constitutional and that the agency and the board have operated in a manner completely consistent with the statutory intent and all state laws.

SCIENTISTS AND PHYSICIANS ARE THE "ACTION HEROES" OF THE 21ST CENTURY

Governor Schwarzenegger, speaking at the Institute's public hearing for "SEED Grants" (exploratory start up grants for brilliant new ideas), called the medical scientists and physicians dedicated to this work, "The Action Heroes of the 21st century". While we can provide the funding and the legal sanctuary for these brilliant scientists and physicians to advance therapeutic research, it is the dedication and commitment of their lives to this new field of medicine that holds the promise of changing the future of treatment of chronic disease. One must remember, as recently as 2003, the U.S. House of Representatives passed the Weldon bill (blocked by the U.S. Senate) which would have criminalized embryonic stem cell research and the scientists and physicians dedicated to this field would have been subject to ten years in prison and $1 million fines. Knowing the recent history and the controversy surrounding the field, for the best and brightest of a generation to commit their careers to this research is extraordinary. For this we are deeply appreciative. We, however, must also remember that in 1977 the last great frontier of medical research—recombinant DNA—was met by protest and ideological attacks often similar to those launched against embryonic stem cell research today. The protesters claimed the research would never lead to medical therapies, in the lifetimes of those living or their children. Because the Federal government did not shut down this research, the first great medical breakthrough came in 1978, from two California institutions, the University of California, San Francisco and the City of Hope National Medical Center. The therapy was artificial human insulin, which keeps my son (who has juvenile diabetes) alive and millions of other men, women, and children alive. In the next decade it led to more than one hundred critical heart and cancer therapies saving tens of thousands of lives, and in the most recent decade it contributed to the knowledge that permitted us to decode the human genome. All of this would have been lost, if funding for this frontier of medicine had been shut down. This is our legacy. The history informs our responsibility for it is now California's opportunity to advance the next great frontier of medicine—stem cell research.

THE RIGHTS OF THE FAMILY AND PATIENTS TO ACCESS NEW THERAPIES

Traditionally, in the United States, the government has assumed the responsibility of funding medical research to drive the development of new therapies that reduce the suffering from chronic and acute disease and injury. The Federal government, at the direction of President Bush, has radically departed from this commitment to pursue one of the most promising areas of medical research that may affect every American family, when his personal view of religion interfered with this advancement. Embryonic stem cell research, specifically, has

From left: Robert Klein, Alan Trounson, Richard Murphy

been suppressed by religious ideology, despite our U.S. Constitution's promise of protection from laws dictated by religion. California has stepped up to the challenge of advancing the stem cell revolution in medical therapies.

INDUCED PLURIPOTENCY OR EMBRYONIC STEM CELL RESEARCH: THE GOLD STANDARD

In 2007, brilliant work by Dr. Yamanaka (originally with the Kyoto University in Japan and now relocating part time to the J. Gladstone Institutes in California) and Dr. Thompson of the University of Wisconsin (also relocating part time to California) identified techniques to convert adult somatic cells to stem cells apparently equivalent to embryonic stem cells, commonly called induced pluripotent stem cells (iPS). While these cells teach us new insights to pluripotency and they may have near term applications for toxicity testing on human cells, it may well be a decade before this technology can be competitive with embryonic stem cells (hESCs). The "artificial" pluripotent cells are derived by transducing genes active in embryonic stem cells but the presence of multiple copies of extra genes can produce unexpected and undesirable outcomes including cancer. It will take some time to address the concerns that must be answered before these new cells can be used for therapies. Despite these extraordinary challenges and risks, the Bush Administration has decided that these cells eliminate the need for embryonic stem cells. They would discard a decade of critical research knowledge on embryonic stem cells that has moved the scientific and medical community to the edge of the first proposed FDA human clinical trial, for acute paralysis, developed through the Reeve-Irvine Research Center at University of California, Irvine, in collaboration with the Geron Corporation. While these trials may take years to perfect, the knowledge developed to launch these human therapies represents an extraordinary value to every family and every patient with the hope of a future stem cell therapy. The breakthrough may actually come through other trials, but the Christopher Reeve trial will mark a milestone in the development of knowledge which will one day make the full range of stem cell therapies possible. The California agency will advance, subject to peer review, the medical understanding of pluripotency, while moving forward to meet its critical mandate to serve patients, who suffer every day, and wait for the earliest, safe and effective therapy to be developed.

CALIFORNIA: A NATIONAL AND GLOBAL LEADER

California has become the largest funding agency in the world for embryonic stem cell research, creating history in funding medical research, as the intellectual health care capital of the society, with long-term state bonds. The vision of the people of California, in approving the California Stem Cell Research and Cures Initiative (Proposition 71), positioned the state as the driving edge of the stem cell revolution in healthcare. Globally, California's performance under Proposition 71 has earned the state agency a world class leadership position, with California serving as a member of the International Stem Cell Forum on an equal membership standing

with 21 member nations. Within the United States, California's grant approvals in 2007 alone are approximately seven times the funding by the National Institutes of Health for embryonic stem cell research (all restricted to pre-August 9, 2001 cell lines). California's medical and ethical research standards, drawn up in collaboration with the National Academy of Sciences, have become an international model and the new "gold standard" for our nation.

ADVANCING THE MISSION

Proposition 71, its governing board, and the funding agency created by Prop 71 face a number of immediate challenges as the momentum of stem cell medical research funding increases including:

First, its initial strategic plan must be examined and strengthened as the new President of the agency, Dr. Alan Trounson, brings global scientific credentials and insights to broaden the strategic path while closing research gaps in the plan which are critical to implementing stem cell replacement therapies for cell therapies in conditions such as Parkinson's Disease, HIV/AIDS, diabetes and heart disease. As an example, strategic initiatives in immunology might broaden the feasible applications of existing adult stem cell therapies, by utilizing embryonic stem cells as a source of immune tolerant cell transplants. Adult stem cell therapies have raised survival rates for patients with leukemia or multiple myeloma (a bone cancer) from six percent to the 70% plus range; but, these therapies generally only reach the 40% of patient candidates for whom a sufficient immune system match can be found. By strategically focusing on the challenges of immunology to expand the reach of adult stem cell therapies, more lives may be saved when scientific breakthroughs in immunology are applied to the objective of immune tolerance of allogenic stem cells and/or to the possibility of immune system matches through SCNT (immune matched stem cells) breakthroughs.

Second, stretching the resources approved by the voters—to fund more research (over time)—by creating a revolving loan fund (to compliment the grant program) could have a dramatic impact on the range of therapeutic advances the agency can fund. The board has just begun phase two of the financial plan by studying how to implement the loan provisions of the initiative. Potentially, a loan program could recycle $1.0 – $1.5 billion—in the first 15-17 years of the agency's life—bringing the total effective resources to fund medical research up to the $4.5 billion range.

Third, the board and the agency need to launch a major public information program, including a specific focus on the upcoming human embryonic stem cell clinical trials. These clinical trials, over time, bring the possibility of remarkable medical advancement, but they also bring the potential for initial tragedies, despite the best safety procedures. Even with the benefit of extensive animal pre-clinical trials, setbacks may occur—particularly given the broad spectrum of therapies and chronic disease challenges. We must respect each patient's decision to take "managed and reasonable" risks that may redeem their futures or save their lives. Medical therapies for the patients in the trials and all future generations are dependent upon the courage of individual patients, if medicine is to advance. With a deep reverence for life, we must inform the California public and every patient about these risks and build the patience and understanding that will be critical elements of medical research risk tolerance. If we are to secure the path to therapeutic success, it will involve many attempts and many "trials". With patience, successful therapies will prove effective.

A HISTORIC OPPORTUNITY

We are all part of a community of patients and families who are dedicated to advancing medical therapy. We understand that research in one area may benefit many areas. Together we will succeed or fail. With a broad spectrum of research, we have a historic opportunity to advance a new frontier of medicine, to reduce human suffering, and to honor the California legacy of medical research, beginning with artificial human insulin from recombinant DNA, which saves my son's life every day.

Robert N. Klein, Chairman,
Independent Citizens Oversight Committee