

# REPORT OF THE EXTERNAL ADVISORY PANEL



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Members of the External Advisory Panel

Interviewees: Grants Working Group, Patient Advocates, Scientists, Industry

## **1. Executive Summary**

Following a unique legislative and financing process, the California Institute for Regenerative Medicine (CIRM) began its operations in 2006. CIRM is an important new paradigm for public support of stem cell research and its translation to clinical development. After approximately six years from the initiative's approval by the voters to implementation, the organization is entering a new stage in its development. As an important part of that evolution from a start up organization, CIRM commissioned an external review of its strategy, policies and procedures.

The purpose of the review was to provide external, objective perspective and advice, to evaluate CIRM's past performance and make recommendations on changes to enable long term success. The External Advisory Panel (EAP), composed of an international group of experts in stem cell research, ethics, and business convened on October 13-15, 2010 in San Francisco and conducted comprehensive interviews with CIRM staff and its Governing Board, as well as interviews with critical stakeholder groups, including grants working group members, patient advocates, scientists, trainees and industry leaders in the stem cell community. In addition, the EAP held open public sessions on days one and three of its review and the entire session with the Governing Board's Chair and Vice Chairs was open to the public. The EAP greatly appreciated the time and effort of CIRM staff and all those who participated in this Review.

The EAP was impressed with this first stage of CIRM's operations. In a remarkably short period of time, CIRM has initiated an ambitious and comprehensive program, ranging from infrastructure support (both facilities and intellectual), the recruitment of a number of excellent young investigators to the state, training of young people, the support of a robust and broad program of research ranging from fundamental biology to preclinical to clinical trials research, strategic international partnerships and the creation of major disease teams focused on bringing novel ideas from the laboratory to the clinic. CIRM's rapid and considerable impact is further evidenced in the conclusion of a recent study by the National Science Foundation which noted that CIRM's \$300 million investment in stem cell facilities, people and programs of research has already been leveraged to more than \$1 billion in support.

The EAP congratulates the State of California for the foresight to create this bold initiative, as well as the Governing Board and CIRM's dedicated and talented staff for the extraordinary and rapid start up of its programs. The EAP also notes that this is an appropriate moment for CIRM to undergo this first external review and to receive outside advice as to how best to deliver on its mandate: CIRM is about to transition from a start up to its next stage of evolution, the founding Governing Board Chair and visionary leader Robert Klein is stepping down and approximately half of CIRM's first tranche of funds have been committed to the programs summarized above.

As CIRM prepares to evolve from a young startup to a maturing organization, the EAP notes that this is a critical time for the organization: critical to ensure orderly transition of Governing Board leadership, critical that CIRM's programs evolve to ensure their alignment with the mandate from the state of California, and critical if CIRM's Governing Board decides to go back to the state of California for further support beyond its initial 10 year mandate.

It is useful to think about CIRM's organizational development of the past few years as Stage I: the Governing Board and staff are in place, many successful programs have been launched, and the impact of these programs is already becoming evident. It is now time for the leadership at CIRM, together with its stakeholders, to agree on future directions in order that CIRM move into Stage II with confidence, clarity, and appropriate programs in place. CIRM's past strategies and programs have established a strong foundation upon which it can undertake this transition. The objective of this transition into Stage II should be to position CIRM and California as a global leader in translating outstanding stem cell science into the clinic, addressing key ethical, economic, regulatory and health delivery issues emanating from regenerative medicine, and delivering health and economic benefit for California.

The EAP has a number of specific strategic recommendations for the next stage, including:

- ***Build on CIRM's previous and ongoing investments***
- ***Sharpen the focus on meaningful, targeted excellence required for global leadership in the development of innovative treatments based on regenerative medicine***
- ***Sustain a vigorous program of fundamental discovery while, at the same time, make critical choices in translating results from the laboratory to the clinic***
- ***Transition to a much more proactive strategy of funding that aligns CIRM's peer review and other processes with its mandate of delivering new treatments to the clinic***
- ***Adopt a porous approach to strategic opportunities, scanning the global environment for scientific advances that have the potential to enrich CIRM's portfolio***
- ***Prioritize the investment portfolio, with input from CIRM's diverse stakeholders***
- ***Build on and expand CIRM's current international strategy, continuing to develop strategic international partnerships that will create both scientific and financial synergies***
- ***Assume a global leadership role in addressing not just the scientific, but also the economic, regulatory, ethical and health delivery issues associated with stem cell research and regenerative medicine***
- ***Expand engagement with the healthcare industry and explore innovative partnerships that will catalyze the movement of research from the laboratory to the clinic***
- ***Increase greatly public awareness within the state and internationally of CIRM's progress on all fronts of regenerative medicine and the potential and realized health and economic benefits, through outreach via patient advocacy groups, grantees and their host institutions, conferences and the internet***
- ***Clarify the roles and responsibilities of the Governing Board and senior management and specifically between the Governing Board Chair and President in order to maximize the likelihood of success of CIRM's mission***

In summary, CIRM has achieved clear and important objective measures of success in its first few years. CIRM now has the opportunity to build on these successes and make the key strategic changes required for continued progress as it transitions into Stage II of its development. California stands out for its boldness of vision in creating CIRM and funding it to scale. With continued strong leadership and vision, outstanding science, and a commitment to partnerships, the EAP believes that CIRM is well positioned to deliver significant health and economic benefits for the State of California.

## **2. History of CIRM**

In November 2004 the voters of California adopted Proposition 71 (the California Stem Cell Research and Cures Act), authorizing the issuance of \$3 billion in state bonds over at least 10 years to support stem cell research in California. The act created the California Institute for Regenerative Medicine (CIRM) and charged the institute with determining the most effective means of distributing state funds to accelerate the science of regenerative medicine and its translation into health and economic benefits for California.

In December 2006, CIRM published its first scientific strategic plan, which served as the blueprint for CIRM's scientific programs and procedures for program implementation. The 2006 strategic plan has served the institute well and has been of enormous value in guiding CIRM to remarkable progress. CIRM re-evaluated the 2006 strategic plan in 2009 to reflect the strategic adjustments to the current state of the field and updates for CIRM's operational model. The purpose of this 2009/2010 strategic plan update, *Accelerating the Opportunities for Cures*, was to build on the solid foundation of the 2006 plan by identifying new research directions for CIRM that reflected the rapidly changing scientific landscape of stem cell science and amalgamate the evolving thinking of CIRM's management and the Governing Board (the Independent Citizens Oversight Committee, ICOC), along with many stakeholders, regarding the most efficient means of implementing CIRM's goals

## **3. Importance of the CIRM Model**

The California Model is an important and innovative new paradigm for public support of stem cell research and therapy development. Stem cell research holds great promise for the treatment of a wide variety of serious diseases and conditions, including type I diabetes, cardiovascular disease, neurodegenerative diseases and spinal cord injury, to name but a few. The financing model that was developed in California is a highly creative approach that acknowledges that the costs of this research should be shared by both today's generation as well as future generations for whom the benefits of this research will likely accrue. Financing by the state also recognizes that the costs and financial risks of this research, especially during the initial seed stages, can only be assumed by the public. The success of this model depends ultimately on the development of novel insights and therapies discovered through stem cell research, and the development of partnerships between the public and private sectors to ensure translation into the clinic.

Over \$1 billion in donor and institutional matching funds provide a strong external validation for the agency's programs and capital structure. Of this \$1 billion, more than \$880 million represent the donor and institutional commitments to the 12 major facility projects and the remainder consists of contributions from the Medical Research Council in the United Kingdom, the Canadian Stem Cell Consortium, and German and Australian funding partnerships. Its seven international collaborative funding partners offer an independent validation of scientific quality and the scientific and financial leverage that derives from these partnerships. In its conclusion, a recent study funded by the National Science Foundation (NSF) stated, "California has established itself as a major center for stem cell research. Recruitment of world-class stem cell scientists from across the globe has been a direct result of CIRM funding." The study summarizes Proposition 71's impact by noting that \$300 million that CIRM has invested in stem cell facilities has already been leveraged to more than \$1 billion in linked donations. This has resulted in significant boosts to the local intellectual communities and has created jobs for the local economies.

## **4. Purpose of the External Review**

As a responsible steward of public funds, CIRM must periodically reevaluate both its funding priorities and operations to stay sharply focused on those research opportunities most likely to achieve therapies and cures. The 2006 scientific strategic plan was intended to be a "living plan — flexible in response to its successes and failures, and opportunistic in capitalizing on unforeseen scientific developments."

Formal assessment by an outside panel and revision as necessary of the 2006 plan was recommended at years three and seven. Year one for the plan was designated to start July 1, 2007, making the first formal assessment due in 2010.

The purpose of the review was to provide external, objective perspective and advice, to evaluate CIRM's past performance, and to make recommendations on changes to enable long term success. The External Advisory Panel (EAP), composed of an international group of experts in stem cell research, ethics, and healthcare business convened on October 13-15, 2010 in San Francisco and conducted comprehensive interviews with CIRM staff and its Governing Board, as well as interviews with critical stakeholder groups, including grants working group members, patient advocacy group representatives, scientists, trainees, and industry leaders in the stem cell community. In addition, the EAP held open public sessions on days one and three of its review and the entire session with the Governing Board was open to the public. The EAP greatly appreciated the time and effort of CIRM staff and all those who participated in this Review.

The stated goals of the evaluation process are:

- Evaluate CIRM's programs against its goals;
- Assess effectiveness in moving CIRM towards meeting its goals and accomplishing its mission;
- Recommend changes in CIRM's funding priorities to ensure that CIRM is supporting the most promising advances in the field of regenerative medicine; and
- Provide other feedback as necessary.

## **5. External Review Agenda**

The EAP received extensive background material from CIRM several weeks in advance of the in-person meeting in San Francisco. CIRM also organized two web sessions for EAP members dedicated specifically to the business issues related to the intellectual property generated by CIRM grantees.

The in-person review was conducted on October 13-15, 2010 in San Francisco at both the Marriott Union Square and CIRM headquarters. Selected portions were open to the public and each day included a time for public comment. The EAP greatly appreciated the time and effort of CIRM staff, Governing Board members, scientists, disease advocates, biotech executives and members of the public who participated in this Review.

### ***Wednesday, October 13, 2010*** ***Interviews with CIRM Staff***

<b>Topic</b>	<b>Key Presenters</b>
Public Meeting	CIRM, Review Panel, Public
Introductions and Overview	Dr. Alan Trounson
Science Base	Dr. Patricia Olson
Evaluation of the Development Portfolio	Dr. Patricia Olson Dr. Bettina Steffen
Operations: Finance Structure, Communications and Education	Dr. John Robson Don Gibbons
Standards, Ethics & Compliance	Dr. Geoff Lomax Ian Sweedler, Esq.
IP Regulations Loan Program	Elona Baum, Esq.
Regulatory Approval Pathway (FDA/EMA)	Elona Baum, Esq.
International Collaborations	Dr. Michael Yaffe Nancy Koch, Esq.
Measuring Effectiveness	Dr. John Robson
Progress Towards 5 & 10 Year Goals Financial Planning	Dr. Patricia Olson Dr. John Robson
Future Strategies	Dr. Alan Trounson Elona Baum, Esq.

### ***Thursday, October 14, 2010*** ***Key Interviews***

- Public Meeting: Office of the Governing Board Chair & Members of the ICOC
  - Board Governance
  - Finance/Bonds/Loans/Legislative relationships
  - Governing Board Responsibilities, Subcommittees and Interaction with Management
- Interviews with Grants Working Group Members
- Interviews with Patient Advocates
- Interviews with Scientists
- Interviews with Biotechnology Companies

### ***Friday, October 15, 2010*** ***Key Interviews***

- Public Meeting (members of the public are invited to give their comments)
- Interviews with Trainees and Scientists
- Review Committee Convenes

## **6. Observations and Recommendations**

### ***Success of CIRM's First Years (Stage I)***

The EAP concluded that CIRM has already delivered extraordinary results in a remarkably short period of time. This accomplishment is especially noteworthy given the limited administrative budget and correspondingly small staff. The agency has awarded 364 grants and loans for research and facilities to 54 institutions totaling \$1.07 billion. About half of those commitments have been disbursed. This progress comes despite several years of litigation and delays. A series of court cases were resolved in CIRM's favor in May of 2007 and the state issued the first bonds under the initiative in October, nearly three years after the vote. The agency was able to fund its first round of grants a year earlier, in April 2006, through a private placement of bond anticipation notes. A year later, a loan from the state's general fund arranged by Governor Arnold Schwarzenegger provided support to allow the acceleration of the second round of funding. To date, the agency has issued 22 rounds of funding. CIRM has established systems and processes for soliciting, evaluating, and monitoring high quality, targeted research projects and has done this in an ethically sound manner. CIRM has established a rigorous peer review process that engages world experts in stem cell research who are called upon for their advice and recommendations. In a short few years, CIRM has created a robust, world class stem cell research effort in California, with a greatly expanded workforce, state of the art facilities and the requisite physical and intellectual infrastructure needed to accomplish its scientific goals. It is now entering a second stage in which it will have the opportunity to build on this solid foundation and deliver on its goal of accelerating research toward the clinic and ultimately to deliver the health and economic benefits for the people of California.

The programs developed by CIRM have already had significant impact on the broader scientific community. As of August 10, 2010, CIRM funding contributed toward research published in 584 journal articles and 23% of those have been in high profile journals, and a CIRM grantee was either a first or last author on 75 percent of all 584 papers. Seventeen shared lab facilities have been built which provide specialized equipment, facilities and training necessary to carry out stem cell protocols. Six of these labs were funded for specific Techniques Training Courses. Of 12 major facilities grants that have been awarded, totaling \$271 million, two projects have been completed and opened this spring, three more were opened in November 2010, two more have been completed and will begin operations by the end of 2010, and all but one of those remaining are scheduled for completion by December 2011. Furthermore, over 100 early to mid-career scientific research leaders have moved to California as a result of these grants, in addition to hundreds of scientists who are post docs and graduate students.

In summary, progress during this first stage of CIRM's development has been remarkable; CIRM has built significant additional research capacity in the state, has attracted scores of talented young people to stem cell research, and has catalyzed large and important stem cell projects across the state. The EAP was most impressed with this rapid start up, the overall quality of the scientists and projects that have been funded, the development of major buildings and other facilities for stem cell research, the forging of several important international partnerships and the innovative training programs that are in place.

### ***The Evolving Model: Driving the Next Stage of Success***

CIRM is now exploring strategies to drive success in the coming years. The key challenge will be to connect and transition the activities and investments in research and discovery of the first stage to a new stage characterized by a proactive strategy, leadership, industry engagement, product development, portfolio prioritization and outreach while continuing to nurture the people and science that will drive the initiative forward. CIRM's initial focus has been to support research at the highest level of scientific excellence. Its challenge now is to continue to support the most promising research while placing increased emphasis on clinical translation and product development. The EAP feels confident that CIRM is poised to build on the success of the first stage to drive further growth towards its long-term mission of providing significant health and economic benefits to the people of California.

### ***Transitioning From a Stage I Start Up to Stage II***

CIRM is approaching its critical sixth year in operation, an appropriate time for the leadership at CIRM, together with its stakeholders, to agree on future directions to move CIRM from Stage I into Stage II with



confidence and clarity of purpose. CIRM's past strategies and programs have established a strong foundation upon which to make this transition. Imminent changes in the leadership of CIRM, including the stepping down of Robert Klein as Governing Board Chair and visionary catalyst of the ICOC, make this an especially challenging time for CIRM. It is absolutely essential at this point to re-visit CIRM's mission and enter Stage II with resolve and commitment to an execution strategy to meet and strive to exceed the expectations of the people of California who boldly supported this initiative.

***Recommendations: Moving the California Institute for Regenerative Medicine Towards Stage II***

In making our recommendations to CIRM, the EAP was guided by the following strategic considerations:

- *The need to preserve the best elements of Stage I while transitioning to Stage II*
- *The need to sustain a vigorous program of fundamental discovery in stem cell science*
- *The need to move away from a traditional funding agency model and adopt a more proactive strategy of funding that places increased emphasis on translational research and the clinical benefits of stem cell science*
- *As an integral part of this proactive approach, to undertake a major portfolio prioritization process involving CIRM's diverse stakeholders*
- *To assume a global leadership role in addressing the technical, economic, financial, regulatory and ethical issues associated with regenerative medicine*
- *To engage industry in exploring innovative partnerships that will catalyze the movement of the research programs from the laboratory to the clinic*
- *As an integral part of this focus on translational research and clinical development, to develop innovative approaches to product development*
- *As a public agency, to increase awareness within the state of California of CIRM's programs of Research and Development*

**The EAP's recommendations are discussed below:**

***Recommendation 1: Maintain Focus on Meaningful, Targeted Scientific Excellence***

CIRM has created a culture of excellence by including experts in all aspects of the organization, particularly in the peer review of grant applications. As a result, CIRM has quickly developed an international reputation for excellence in science coupled with the strong underlying principle that the research funding needs to be aligned with the mission of CIRM. We strongly encourage CIRM to maintain this standard of excellence in all aspects of its work, programs and investments. The public trust in CIRM and the ability of CIRM to develop international and industry partnerships depends on the quality of its staff and the choices of programs it supports. We note that the members of the Grants Working groups that we interviewed were particularly complementary of the quality of the peer review mechanisms that CIRM has put in place, noting that the emphasis is on impact and innovation, the forms are not onerous (except for the budget pages), and the quality of the proposals are, in general, very good to outstanding.

***Recommendation 2: Sustain Fundamental Discovery***

Stem cell research is still in its early stages and there remain many fundamental concepts to be discovered. CIRM has to be a major contributor to the global effort to understand the biology, developmental plasticity and potential of various types of stem cells and to develop strategies to manipulate the developmental program of these cells. Therefore, the basic biology programs are the fuel that will continue to drive discovery and innovation in stem cell research and to create new opportunities for applying the unique properties of these cells to the clinic. We strongly encourage CIRM to continue to invest in the research programs, intellectual infrastructure, training and development necessary to advance the understanding of stem cells.

***Recommendation 3: Paving a Path from Fundamental to Translational Research, Translational Medicine, Product Development and Healthcare Delivery***

In the first stage of its programs, CIRM relied largely on responses to calls for proposals, and funded those projects that were most scientifically and programmatically meritorious. A reactive approach was entirely appropriate in Stage I. Now, however, CIRM needs to evolve to ensure that it can successfully deliver on its mission to develop innovative therapies for human disease and injury through stem cell

based therapies. In this second stage, we encourage CIRM to increasingly move away from a traditional funding agency model and adopt a more aggressively proactive approach to identifying innovative projects across the stem cell therapeutic landscape that show promise for moving into translational research, clinical trials and product development. This strategy will require an exhaustive strategic assessment of projects ongoing both inside and outside of CIRM, as outlined below in Recommendation 4.

Senior leaders from the California biotechnology industry stressed in their meeting with the EAP the critical role of industry in moving innovative ideas from the laboratory to clinical trials and eventually into clinical practice. The EAP believes that industry needs to play an increased role during Stage II of CIRM's programs. At the same time, the precise role of industry needs to be explored and defined. As it is unlikely that one size will fit all, CIRM has an opportunity to evaluate various healthcare delivery models and to lead a global discussion on how best to translate the results of fundamental stem cell research from the lab into the clinic. Although industry has played a relatively modest role relative to academia in translating bone marrow transplantation from experimental animal models into standard clinical practice in tertiary clinics throughout North America and Europe, industry has expertise in protein and cell manufacturing and clinical development that will be invaluable in defining new business models for delivering stem cell based therapeutics. Industry must be fully engaged in Stage II.

Overall, in this new stage, CIRM has the opportunity to retain the excellent features of Stage I, and build on them, in transitioning to Stage II. In so doing, CIRM must depart from a traditional granting agency paradigm and become proactively focused on clinical translation, product development and healthcare delivery.

***Recommendation 4: Portfolio Prioritization Process***

An important part of a CIRM Stage II strategy is the critical evaluation of the projects funded during Stage I. We encourage CIRM to conduct a critical assessment of its current portfolio. Advised by a group of outside interdisciplinary experts, the review should have carefully selected objective benchmarks, and have, as its primary goal, the identification of programs that should move forward and those that should not. Additionally, while the EAP appreciates the natural wishes of disease groups to move forward on particular diseases or conditions, CIRM's Governing Board, guided by management and external advisors, must begin the difficult process of focusing the number of disease areas to those that it believes have the greatest chance of development progress and clinical success, given reasonable timelines and budget. Attempting to move forward across too broad a front might compromise moving forward on any disease. Undoubtedly, these will be difficult decisions; however, CIRM's Governing Board has the inclusive composition and the demonstrated wisdom to begin these critical discussions.

***Recommendation 5: Develop an Open Innovation, Porous Pipeline Strategy***

The review group noted that CIRM had chosen an internal pipeline model for achieving clinical success for its major goal of reaching human proof of concept for one application of regenerative medicine. This internal pipeline model, akin to CIRM being its own pharmaceutical company, utilizes an attrition model to determine how many preclinical translational projects need to be funded to result in a given number of successful INDs which in turn would result in a predicted number of Phase I safety trials in humans, which would finally yield a small number of Phase II human proof of concept trials, at least one of which would be predicted to be successful. The attrition model predicts a certain rate of failure at each of these steps which was used to drive the number of early translation projects funded. The EAP recommends an alternative model for success that allowed the most likely source of clinical projects to come from either inside or outside of CIRM funded research, perhaps out of industry and even from outside of California. CIRM funding might be much better spent on having available resources to capture these projects and bring them to California under CIRM funding to California collaborators and that these projects could enter the CIRM pipeline at any stage of preclinical or clinical development. We would refer to this as a porous opportunity model rather than an internal pipeline model. The EAP felt that this was an approach that was much more likely to yield success, would be most responsive to scientific opportunity and would keep California as the hub for clinical proof of concept in regenerative medicine for the world rather than just for CIRM funded pipeline projects.

***Recommendation 6: Social, Ethical, Health Care Delivery and Regulatory Issues***

To our knowledge, the combination of CIRM's mandate and budget make it a unique enterprise globally. As the world enters a new era in which stem cell based therapies create novel paradigms for treatment, CIRM has the opportunity and perhaps even the exceptional responsibility to assuming a leadership role in both stem cell research and the crucial discussions prompted by the research. For example, CIRM has initiated informal discussions with regulatory officials to explore the pathways that must be taken to obtain regulatory approval for stem cell based therapies. There are critical ethical, economic, manufacturing, health delivery, and social issues that require research, discussion and translation into policy and practice. These activities should be viewed as an integral part of CIRM's portfolio.

***Recommendation 7: Industry Engagement***

Biopharmaceutical industry involvement in CIRM is critical to its success. Nevertheless, while CIRM has attempted to engage industry with some limited success, it is clear that considerable obstacles to industry engagement remain. For example, the majority of granting processes are designed on academic models. These processes do not necessarily fit the needs or timelines of industry and/or the realities of managing industry projects. Granting processes and funding criteria could be clarified and streamlined from an industry perspective and timelines for decision-making could be aligned with industry norms. While CIRM's loan program is intriguing, the details of loan repayment and options need simplification and do not appear to be attractive to industry. In summary, the EAP felt that there is now a critical opportunity for new thinking to ensure serious engagement with industry.

The EAP suggests that CIRM convene an industry advisory panel to meet with CIRM management to discuss the issues above and other issues as they arise.

***Recommendation 8: International Partnerships***

The EAP is highly supportive of the emphasis on international partnerships that have characterized CIRM's early years. These partnerships have leveraged outside scientific expertise and resources. They have also served as an ambassador, allowing the global scientific community to see firsthand the progress being made in California as a result of CIRM and its programs of research. The EAP encourages CIRM to broaden these partnerships to other regions and countries and to diversify the partnerships beyond other stem cell communities into those areas of science that have the potential to support CIRM's mandate.

***Recommendation 9: Outreach and Education***

Thirty-five years ago, California led the world in the development of the science behind genetic engineering and recombinant DNA technology and in engaging and ensuring that the public had the opportunity to meaningfully participate in a dialogue about its uses and its limits. Today, the opportunities in stem cell based therapies are no less exciting and important. CIRM has the opportunity and a special responsibility to report to the citizens of California on the progress, activities and challenges of the organization. Given the innovative mechanism by which CIRM is funded, and the particular nature of the research that it funds, the EAP strongly encourages CIRM to significantly increase both the quality and breadth of its community outreach and education programs. The objective should be to ensure state-wide visibility and awareness of the contributions that California is making to the global research effort and to create opportunities for Californians to be informed about advances in the research, and to engage in dialogue with the scientific and clinical community about the benefits, limits and resulting guidelines for this exciting area of biomedicine.

***Recommendation 10: Governing Board Composition and Corporate Governance***

The CIRM Governing Board has had a very hands-on approach to CIRM in its first six years. This approach is appropriate for start ups, especially one that is publicly funded and accountable such as CIRM. As CIRM transitions to Stage II, we believe this is an appropriate time for the Governing Board to examine its role and composition, mindful of the legal reporting, fiduciary and accountability requirements of the state of California. With the imminent stepping down of the founding Governing Board Chair and CIRM visionary Mr. Robert Klein, it is imperative that the roles and responsibilities of the Governing Board Chair and CEO positions remain distinct but

complementary to ensure the continued positive, collaborative partnership between these two key individuals. There should be clarity of the roles and responsibilities of the Governing Board Chair and CEO as it pertains to CIRM's strategic directions, its policies, international partnerships, funding decisions, public communications and oversight.

***Other Recommendations***

*Streamlined Processes.* CIRM should consider a more flexible project funding process with less administrative documentation and rolling funding cycles. This would allow for innovative projects to be captured in the CIRM portfolio, particularly from industry, that may not fall within the established RFA cycles.

*Resources.* By any standard, CIRM has an exceptionally lean internal infrastructure in terms of administration, staff and other support. In the next stage, CIRM will need to expand its internal capabilities to allow the organization to take a more proactive approach to investment, portfolio optimization, industry engagement, product development, and community outreach.

## **7. Benchmarks for Future Success and Concluding Comments**

In summary, this first stage of CIRM's development has been impressive, building significant research capacity in the state of California, reaching out to attract young people from diverse backgrounds to participate in stem cell research and creating large and key stem cell projects across the state.

We propose the following ten points as objective benchmarks of success toward CIRM's ultimate goal of finding cures for devastating diseases:

1. Continued investment in intellectual infrastructure and fundamental discovery
2. Continued advancements in human disease models using stem cells
3. Inclusion of development and translational research programs moving towards human clinical trials in CIRM's portfolio
4. Integration of ethical, economic, manufacturing, health delivery, and social issues research for translating discoveries into practice and policy
5. Active industry participation in CIRM activities
6. Development of a more open innovation model in which CIRM's investments are leveraged by the best advances anywhere
7. Adopting an even more ambitious international strategy, forging strategic partnerships with academic and industry groups around the world
8. Convening of international stem cell organization and external organizations to engage in a dialogue on best practices
9. Development of business models for regenerative medicine
10. Public engagement and dialogue in this new era of regenerative medicine

The EAP believes that, with the implementation of the recommendations discussed in this report, CIRM has the unprecedented opportunity to be a global leader in stem cell science and its application to the practice of medicine. Advances in stem cell science have the potential to transform the treatment of many serious and life-threatening diseases and injuries that affect millions of people in California and around the world. California stands out for its boldness of vision in creating CIRM. CIRM's next 5 years must continue to reflect that boldness of vision. With strong vision and leadership, combined with funding to scale, outstanding science, and partnerships with California's great universities, industry, and international organizations, CIRM has the potential to create significant health and economic benefits for the people of the State of California.

## **9. APPENDIX: Members of the External Advisory Panel**

**DR. ALAN BERNSTEIN (PANEL CHAIR)** is the Executive Director of the Global HIV Vaccine Enterprise and former President of the Canadian Institutes of Health Research.

**DR. GEORGE DALEY** is director of Stem Cell Transplantation and the Samuel E. Lux IV Professor of Hematology/Oncology at Children's Hospital Boston and Dana Farber Cancer Institute, and Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School.

**PROFESSOR SIR MARTIN EVANS** is a Nobel Laureate for his work on embryonic stem cells, President of Cardiff University and Professor of Mammalian Genetics at Cardiff University.

**DR. IGOR GONDA** is the President and Chief Executive Officer of Aradigm Corporation, a public biopharmaceutical company in California specializing in the prevention and treatment of severe respiratory diseases.

**DR. JUDY ILLES** is the Canada Research Chair in Neuroethics, Director of the National Core for Neuroethics at the University of British Columbia, Professor of Neurology, and Adjunct Professor with the School of Population and Public Health.

**DR. RICHARD A. INSEL** is Chief Scientific Officer for the Juvenile Diabetes Research Foundation.

**DR. RICHARD KLAUSNER** was formerly the executive director of the Program in Global Health at the Bill and Melinda Gates Foundation's, former director of the National Cancer Institute (NCI) and is a managing director of The Column Group.

**DR. NANCY WEXLER** is the Higgins Professor of Neuropsychology in the Departments of Neurology and Psychiatry of the College of Physicians and Surgeons at Columbia University, as well as the President of the Hereditary Disease Foundation.

**MS. SAIRA RAMASASTRY (ADVISOR TO THE EAP)** is a Managing Partner at Life Sciences Advisory, LLC, a strategic advisory services firm focused on the emerging biopharmaceutical industry.

## 8. APPENDIX: Grants Working Group Participants

### Grants Working Group Participants

CONFIRMED			October 14th from 12:00 to 1:30pm Pacific
by phone	Charles Stiles, Ph.D.	Professor of Microbiology and Molecular Genetics, Harvard Medical School	Dana-Farver Cancer Institute, Harvard Medical School
by phone	Susan Bonner-Weir, Ph.D.	Senior Investigator, Joslin Diabetes Center; Associate Professor, Harvard Medical School	Joslin Diabetes Center
by phone	Paul Simmons, Ph.D.	Professor & Director, Centre for Stem Cell Research; President ISSCR	Brown Foundation Institute of Molecular Medicine at UT, Houston.
by phone	Rainer Storb, M.D.	Clinical Research Division, Head, Transplantation Biology Program, Fred Hutchinson Cancer Research Center; Professor, Medical Oncology Division, University of Washington School of Medicine	Fred Hutchinson Cancer Research Center & University of Washington School of Medicine
by phone	Mark Furth, Ph.D.	Science Officer at Wake Forest Institute for Regenerative Medicine and Technology Development Officer at Wake Forest University School of Medicine	Wake Forest University
in person	Ali Brivanlou, Ph.D.	Robert and Harriet Heilbrunn Professor, Laboratory of Molecular Vertebrate Embryology	The Rockefeller University

## **8. APPENDIX: Patient Advocate Participants**

### **Patient Advocate Participants**

<b>CONFIRMED</b>		<b>October 14, 2010 1:30 to 3:00pm</b>
in person	Diane K. Winokur, National Board Trustee	The ALS Association
in person	Don Reed	Sponsor, Roman Reed Spinal Cord Injury Research Act; Co-chair, Californians for Cures; Vice President, Public Policy, Americans for Cures
in person	Judy Roberson, President	Huntington's Disease Society of America Northern California Chapter
in person	Loren Leeds	HIV/AIDS, AIDS-related lymphoma patient
in person	Mark Fischer-Colbrie, former President, Greater Bay Area Chapter, JDRF National Speaker's Program	Juvenile Diabetes Research Foundation
in person	Sophia Colamarino, Vice President, Research	Autism Speaks
in person	William Remak, Chairman	California Hepatitis C Task Force & National Association of Hepatitis Task Forces.
by phone	Theresa Blanda	Blood disorder patient advocate
by phone	Stephen Rose, Ph.D., Chief Research Officer	Foundation for Fighting Blindness



## 8. APPENDIX: Research Scientist Participants

### Research Scientist Participants

CONFIRMED			October 14th from 3:30 to 5:00pm Pacific
by phone	Dennis Clegg, Ph.D.	Co-Director of the UCSB Center for Stem Cell Biology and Engineering.	University of California, Santa Barbara
by phone	Irving Weissman, M.D.	Director, Stanford Institute of Stem Cell Biology and Regenerative Medicine, Comprehensive Cancer Center, and Stanford Ludwig Center for Stem Cell Research at Stanford; V&D Ludwig Professor of Clinical Cancer Research; Professor, Pathology, Developmental Biology, and by courtesy, Neurosurgery and Biology	Stanford University
by phone	Larry Goldstein, Ph.D.	Professor of Cellular and Molecular Medicine at the University of California, San Diego, School of Medicine, HHMI Investigator	University of California, San Diego
by phone	Owen Witte, M.D.	Professor of Microbiology, Immunology, and Molecular Genetics; Professor of Molecular and Medical Pharmacology at the David Geffen School of Medicine and Founding Director of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research and HHMI Investigator	University of California, Los Angeles
in person	Catriona Jamieson, M.D., Ph.D.	Assistant Professor, Medicine, Hematologic Malignancies Program	Moore's Cancer Center, University of California, San Diego
in person	Deepak Srivastava, M.D.	Director, Gladstone Institute of Cardiovascular Disease; Professor, Departments of Pediatrics and Biochemistry & Biophysics; Wilma and Adeline Pirag Distinguished Professor in Pediatric Developmental Cardiology	The Gladstone Institutes
in person	Jan A. Nolte, Ph.D.	Stem Cell Program Director, UC Davis Institute for Regenerative Cures	University of California, Davis
in person	Jeff Blustone, Ph.D.	UCSF Executive Vice Chancellor and Provost; AW and Mary Clausen Distinguished Professor of Medicine, Pathology, Microbiology & Immunology	University of California, San Francisco
in person	Ken Weinberg, M.D.	Professor, Pediatrics - Stem Cell Transplantation & Member, Cancer Center	Stanford University
in person	Peter Donovan, Ph.D.	Director, Sue and Bill Gross Stem Cell Research Center Department of Biological Chemistry, Department of Developmental & Cell Biology Molecular Genetics of Germ Cell and Stem Cell Development	University of California, Irvine

## **8. APPENDIX: Industry Participants**

### **Industry Participants**

<b>CONFIRMED</b>		<b>October 14th from 5:00 to 7:00pm</b>
by phone	Joydeep Goswami, Ph.D., M.B.A., Vice President, Primary & Stem Cell Systems	Life Technologies
by phone	Michael West, Ph.D., CEO	BioTime, Inc.
by phone	Tom Okarma, M.D., Ph.D., President and CEO	Geron Corporation
in person	H. Ralph Snodgrass, Ph.D., Founder, President and CSO	VistaGen
in person	John Walker, Senior Advisor	iPierian, Inc.
in person	John West, M.B.A., CEO	ViaCyte, Inc. (Novocell)
in person	Ken Stratton, J.D., M.B.A., General Counsel	Stem Cells, Inc
in person	Martin McGlynn, President and CEO	Stem Cells, Inc
in person	Michael C. Venuti, Ph.D., President & CSO	iPierian, Inc.
in person	Phillip Gregory, D. Phil., CSO	Sangamo

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## **8. APPENDIX: Trainees/Scientists Participants**

Xianmin Zeng, The Buck Institute

Josh Elias, Stanford University

Archana Shenoy, UCSF Trainee

Kitman Yeung, San Francisco State University Bridges Student

Jason Liu, San Francisco State University Bridges Student

Nicole Haste, San Francisco State University Bridges Student