MEMORANDUM

Date: March 14, 2013

From: Alan Trounson, PhD
CIRM President

To: Independent Citizen's Oversight Committee

Subject: Extraordinary Petition for Application ID1-06617 and IR1-06595

Enclosed is a petition letter from Dr. Stephen Chang and Susan Solomon of the New York Stem Cell Foundation, an applicant for funding under RFA 12-04 and 12-03, CIRM hiPSC Repository Awards and Derivation Awards. This letter was received at CIRM on March 13, 2013 and we are forwarding it pursuant to the ICOC Policy Governing Extraordinary Petitions for ICOC Consideration of Applications for Funding.

NYSCF
The New York Stem Cell Foundation

The NYSCF Research Institute
An Opportunity to Revolutionize Medical Research

NYSCF Response to CIRM Reviews [RFAs 12-03 and 12-04]

Dear Members of the Independent Citizens' Oversight Committee:

The New York Stem Cell Foundation (NYSCF) was founded in 2005 by Susan Solomon, a patient advocate with a son with type 1 diabetes, to accelerate cures and treatments for patients through the use of stem cells. From the start, the major focus of NYSCF has been the generation of human pluripotent stem cell lines. This has included the generation of the first-ever patient specific stem cell line from a patient with ALS in 2008, the generation of the first-ever patient specific embryonic stem cell line in 2011, and just this past December the discovery of a cure for maternally inherited mitochondrial diseases using stem cell techniques. This has now culminated in the establishment of the first of its kind, a state-of-the-art, automated system for high-throughput derivation of human iPSCs, which we proposed to use for the generation of the 9000 lines requested by CIRM in the current RFAs. Importantly, this technology allows us to maintain the highest level of characterization required to ensure the greatest utility of the lines produced under this RFA.

We are very pleased that both of our applications (**ID1-06617** for derivation of hiPSCs and **IR1-06595** for establishing an iPSC repository) were "***provisionally recommended for funding***" by the Grants Working Group. The reviewers recognized that "*automation represents the future of large-scale hiPSC generation and its use is a strength of the application.*" While the reviewers raise a concern that the use of automation is "*not yet routine*" – we are happy to report that we now have the systems operating near capacity, and are producing over 200 lines per month. While automation is not yet routine for any other group, our fully automated system is exactly what sets our application apart from the others. The success of these efforts is evidenced by our interactions with leading researchers in the New York area and in California. Letters from collaborators Drs. Marc Tessier-Lavigne, Xianmin Zeng, and Samuel Gandy who have proposed the use of this system in their large-scale iPSC programs will be provided prior to the board meeting. Their proposals document the success of existing collaborative efforts that utilize our automated facility. As leaders in this space, these investigators recognize the value of integrating cutting edge technology to ensure the future success of their programs. Recognizing CIRM's commitment to innovation, creative solutions, and new technology, we believe that our proposal to use new automation technology is in line with these goals, and will provide the latest and most effective technology to California's stem cell programs.

Many of the reviewers' comments were insightful and helpful. Specifically, we agree that "*passaging methods*" and "*the clone selection process could impact the quality of the resulting hiPSC lines*". To address this particular point, we provided detailed information within our application on all of our specific operating procedures, including protocols for passaging and clonal selection. These procedures enable high-throughput derivation of the hiPSC lines while maintaining the integrity of the cell lines, and establishing strict criteria for cell characterization.

The reviewers were concerned that "*evidence of the ability to perform large-scale derivations is still lacking*". It should be pointed out that we are the first and only group to have established completely automated production of iPSC lines, and our ability to ramp up production is improving rapidly. We are now producing, on average, 48 iPSC lines per week, and we have established a collection of over 300 iPSC lines. The viability of our program is supported by the growing confidence and continued use of these cell lines by our collaborators; notably, numerous groups have signed on to use the system in their future research efforts, including groups led by Drs. Tessier-Lavigne, Zeng, and Gandy who have provided letters of support referenced above. We hope that CIRM support will enable many more Californian investigators to join this group in setting new standards for quality and reproducibility of cell lines, sponsored through this initiative.

The reviewers thought that the space we identified is too small, and insufficient for the proposed programs. We wish to point out that the proposed system for our automated process requires a much smaller facility compared to standard cell culture programs. The footprint and operating space of our current automated system is less than 2,500 sq. ft. Our proposal to lease a 7,050 sq. ft. facility for the CIRM program (including shared support facilities for both the proposed Derivation and Repository Programs) is more than adequate for the functions described. If more space is needed as the facility develops, we can rapidly obtain more space with little impact on our overall budget. The proposed facility is located in a building that also houses Gladstone and UCSF laboratories funded by CIRM. We have identified an additional 4,600 sq. ft. of space in the proposed location that is currently leased by the Gladstone, and they have indicated that this additional space is available if needed (letter will be provided prior to the board meeting).

As the reviewers noted, the "*proposed hiPSC derivation platform would benefit from being established in one of the key CIRM-funded institutes; this would enable technical exchange and sharing expertise*". We agree with this point, and have provided letters from the following investigators in California who support our automation platform and express great interest in collaborations with us. These letters indicate the strong interest in technical exchange and expertise sharing to ensure that our Derivation and Repository programs would benefit from the growing wealth of knowledge in California, and how these investigators would benefit from interactions with us. The list of investigators includes:

- Kristin Baldwin (Scripps)
- Dennis Clegg (UCSB)
- Peter Coffey (UCSB)
- Sheng Ding (Gladstone)
- Fred Du Savage (Genentech)
- Larry Goldstein (UCSD)
- Arnold Kriegstein (UCSF)

Regarding our program director and leadership, we are delighted that the review committee recognized that the "*scientific leadership of the applicant institution is world-renowned, with expertise in stem cell applications and in automation, liquid handling and quality control of cells.*" Our goal is to bring this expertise to California. We are prepared to fully staff the California facility with already-trained NY personnel, who will remain until the California team is hired and fully trained. By hiring Californians to staff our new facility, we will be expanding the training of new staff within the state, and at the same time providing employment to California citizens with CIRM funding. The PI currently resides in California, and we have already identified potential lead staff, who are currently California residents.

A final point was made regarding a lack of sufficient information on equipment purchases required to establish the automated platform. At this point, this information is proprietary. We would be happy to provide detailed, confidential information to CIRM staff.

In closing, we are very enthusiastic about the possibility of working with CIRM to bring our state-of-the-art iPSC production program to California for the derivation and maintenance of the 9000 lines created through the RFAs. The CIRM awards provide an opportunity to facilitate standardized production criteria for hiPSC lines and ensure that they are broadly available, free of commercial restrictions. These goals align perfectly with our mission. Please do not hesitate to contact us with any questions or for further clarification on any issue.

Sincerely,

Stephen Chang, PhD
Vice President of Research and Development

Susan Solomon, JD
Chief Executive Officer