CEDARS-SINAI
HEART INSTITUTE

EDUARDO MARBÁN, M.D., PH.D.
DIRECTOR

March 12, 2014

Members and Alternates, ICOC, CIRM

RE: DR3-07201

Dear ICOC members:

As Principal Investigator of the abovecited Disease Team application, I would like to share with you some comments regarding the proposal, upon which you will act tomorrow.

1) I am a cardiologist whose life work is dedicated to making regenerative medicine a clinical reality. My team was the first to show that therapeutic regeneration is possible in humans: in the CADUCEUS trial [*Lancet*, 2012], we were able to regrow healthy heart muscle in patients whose hearts were previously believed to be irreversibly scarred. Although CADUCEUS was conducted without CIRM funds (the study was NIH-funded), the potential power of CIRM to bring cures to the public was a significant motivator in my move to Cedars-Sinai after 25 years at Johns Hopkins. Soon after my arrival in California I procured a Disease Team from CIRM; that became ***the first CIRM grant to deliver a validated, FDA-approved therapeutic candidate.***

2) The clinical program around that therapeutic candidate is now being studied in a phase 2 clinical trial (ALLSTAR). ***This clinical program is far ahead of any other CIRM-funded program in terms of human testing.***

3) The commercial potential of that product has been validated by a collaborative/option agreement between Capricor (the company I founded to develop regenerative therapeutics) and Janssen, an arm of the pharmaceutical giant Johnson and Johnson. This represents the first time that "big pharma" has partnered with a regenerative medicine biotech to develop a product.

4) ***The present proposal (DYNAMIC) is ready to go into patients immediately***; it is FDA and IRB approved. In fact, we have a list of 30+ patients who are waiting to be screened for enrollment, as soon as funds are available. These patients are ill, with a mortality exceeding that of many cancers. Indeed, several eligible patients have died in the interlude between the last ICOC meeting, when this proposal might have been funded, and the present.

5) DYNAMIC would be the first study in the CIRM portfolio to target hard clinical endpoints (mortality and re-hospitalization) in a very high-risk population (that of advanced heart failure). ***The population to be studied is very different, and much sicker, than in the ALLSTAR trial.***

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6) The therapeutic candidate has now been administered to 14 patients in the phase 1 safety arm of ALLSTAR. That trial that has met its primary endpoints and has received formal NIH and IRB approval to proceed to phase 2, which is currently under way at multiple centers.

7) The initial review was tainted by conflict of interest concerns. ***The re-review was conducted by staff in a peremptory manner without the usual CIRM due process***: no patient advocates were involved, no comparator grants were evaluated, and no formal review reports have been provided. Only a pithy, dismissive summary by CIRM staff has appeared, and that only yesterday.

8) Under circumstances such as these, ICOC has the opportunity to overturn negative recommendations based on flawed reviews, in the interest of proceeding with studies that may benefit the citizens of California. I have delivered in every promise that I have made to CIRM before, and I will do so again if given the chance. It is lamentable that scientific members from grantee institutions are unable to participate fully in the vetting process for such applications, in light of IOM recommendations. What we need in situations such as this one is more transparency and more informed discussion, not less.

Given all these considerations, I respectfully urge the ICOC to approve DR3-07201 for funding.

Sincerely,

Eduardo Marbán, MD, PhD

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