March 20, 2015
Independent Citizens Oversight Committee (ICOC)
California Institute of Regenerative Medicine
Re: PC1-08105

I write to address the Committee about our proposal entitled Preclinical development of a WNT activated autograft containing endogenous stem cells to enhance skeletal healing. There are 6 reasons why we believe this proposal should be funded.

1. CIRM guidance and ICOC support have shaped this program for 7 years

- Our program began in 2009 as the highest ranked Early Translational award
- In 2013 CIRM staff supported, and ICOC approved, the first-ever Bridging funding because of the "mission critical status of the project, …its competitiveness, and (our) performance against milestones"
- In a continued vote of confidence from CIRM staff and the president, we received in 2014 Extraordinary Supplement funding based on accomplishing the milestones outlined in the Bridge funding, and on "advice from external independent reviewers and internal discussion".
- Our median score for this proposal is 75 and the majority of Reviewers recommended funding. In addition, our program received strong internal support from CIRM programmatic staff.

2. The program aligns with CIRM objectives

- We address an unmet medical need in an underserved -and often overlooked- patient population; namely, the aged. Ours is the only program that specifically focuses a stem cell-based therapy to improve skeletal healing in the elderly. Elderly patients are entitled to the same level of healthcare afforded to younger patients; consequently, it is incumbent upon CIRM to support clinically viable therapies that help this rapidly growing sector of our population.
- CIRM wants to support efficacy and accelerate development of stem cell therapies. Our partnership with Avalon Ventures epitomizes this vision, as embodied in the formation of Ankasa Regenerative Therapeutics. The entire Stanford/Ankasa team combines the rigor of seasoned investors with a world-class advisory team and is focused on the most efficient, effective use of resources to quickly deliver a safe stem cell therapy to Californians.

3. The program plan is sound, and will accelerate new treatments for patients

- Reviewers had nothing negative to say about the proposed product, the preclinical data, the approach, the veracity of the indications, the MOA, the proposed plan of action, or the milestones. Their primary concern was that we focus on a single indication.

"Selection of first-in-human target indication", the CIRM 14-02 webinar[1] states, "is *in scope*". Therefore, we believe it is unfairly punitive to criticize us for following guidance in the RFA. Further, reviewers commented on our "well-documented Milestone Plan", which clearly identifies lead indication selection as an early objective.

- Reviewers suggested that we would "strongly benefit from a qualified regulatory expert" and "earlier FDA engagement is critical for establishing a path to IND".

[1] http://www.cirm.ca.gov/files/files/RFA%2014-02%20webinar_final.pdf

We strongly agree; our Milestone Plan clearly indicates a pre-pre-IND meeting in the first 9 months, which according to the CIRM webinar, is *in scope*. Further, our team already includes RRD International, a highly competent and well-respected organization that has provided experienced, regulatory-driven product development support for hundreds of products.

4. CIRM staff concur: the program is poised for commercialization

- I was invited by CIRM to speak at Stem Cell meeting on the Mesa in both 2013 and 2014. This partnering forum connected a select few CIRM projects with major industry players, big pharma, and investors with the goal of speeding commercialization.
- I was invited as one of CIRM's four panelists to speak about our program at the Milken Institute Global Conference in 2014. Each year, this think-tank convenes a network of influential decision-makers to address the most urgent challenges facing healthcare.
- We have received continual guidance from CIRM's business development office, which has aided our ability to raise significant external capital.

5. We are the highest ranked proposal with California-based venture co-funding

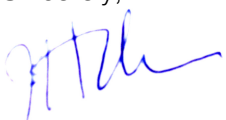
- RFA 14-02 (Section III.B), states, "CIRM will prioritize projects that have received prior CIRM funding and which are able to demonstrate co-funding equivalent to at least 25% of the amount requested from CIRM."

Avalon's founding and managing partner, Kevin Kinsella, has followed this program for almost 4 years. He has gotten to know the Stanford team, our external advisor David Lacey [former SVP of Research at Amgen], the science, and the milestones. As a demonstration of their commitment, Avalon founded Ankasa Regenerative Therapeutics in 2014. Ankasa is now raising $16M -well above the 25% threshold- toward funding through Phase I.

6. The majority of PC Reviewers recommended funding

Historically, staff and the ICOC have recognized that the average score is not the sole criterion for funding. For example, in the last ICOC meeting a median score of 75 and a majority of reviewers placing the application in Tier 1 was a central rationale for moving applications from Tier 2 to funding[2]. Our proposal satisfies both criteria.
Based on this precedent, the priority promised to PC programs with co-funders, and the data presented herein, we respectfully request funding approval by the ICOC.

Sincerely,



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[2] https://www.cirm.ca.gov/sites/default/files/files/agenda/150129_Agenda_7_TnT_Review_Summaries.pdf