City of Hope™

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May 13, 2024

Application Review Subcommittee (ARS)
Independent Citizens Oversight Committee (ICOC)
California Institute for Regenerative Medicine (CIRM)

Re: TRAN1-16192: Targeting Pancreatic Cancer with Allogeneic Off-the-Shelf PSCA-CAR NK Cells

Dear Committee Members and Administrative Team for CIRM:

I am writing to request funding for TRAN1-16192 during the current review cycle. We are in a unique position at the current time to accelerate our "off the shelf" PSCA CAR NK cells secreting IL15, derived from CD34+ cells, to treat pancreatic cancer, a devastating disease without known cure. Pancreatic cancer is the third leading cause of cancer-related death in California and has the lowest 5-year overall survival rate for any cancer of only 9%. Except when diagnosed early as an incidental finding (≤ 10% of the time), it is uniformly fatal without significant advances in therapy over the past 50 years. Thus, novel therapies are needed. Importantly, it disproportionally affects Black Californians and is increasing at an alarming rate in the American Indian/Alaska native population in California.

After searching the CIRM funding portfolio, we found that only four projects target pancreatic cancer, three active and one closed. However, all are at an early discovery stage (one DISC0 and 3 DISC2). If our TRAN1 project is funded, it will be the one closest to advancing to the clinical stage for this dreaded disease.

Overall, the review of our TRAN1-16192 CIRM proposal was very positive, and we received a median score of 88. The majority of the review panel members (10 out of 14) voted for funding. All reviewers (12 out of 12) agree that our proposal is "well planned and designed" and "feasible" as well as "upholds principles of DEI" in three of the five scoring categories. Our product is a cryopreserved, "off the shelf", unmatched allogeneic PSCA CAR NK cell secreting IL15 derived from any donor's CD34+ stem cells, which are safe and effective in our published and unpublished preclinical models. Importantly, the cryopreservation technology and random allogeneic donor allow scale and drive the cost significantly lower than CAR T cell therapy, further improving access to all populations. The GWG members expressed enthusiasm for these advantages.

As the GWG review committee commented, we have "a strong team with a good track record and support from the host institution". We have previous experience translating engineered NK cells to a Phase I clinical trial in about three years to treat lung cancer (NCT05334329), although those NK cells do not have a CAR. Like the engineered NK cells now being used to treat lung cancer in NCT05334329, we have provided strong evidence that our PSCA CAR NK cells secreting IL15 do traffic to both the primary organ (pancreas) and to sites of metastatic disease.

Importantly, we are grateful for the feedback we received regarding our plan for DEI (attached). Consequently, we have vastly restructured our strategic approach for this TRAN1 preclinical project that will allow us to: (1) increase workforce diversity and, (2) increase cultural competency training to better promote inclusion in the workplace. To do so, we will team up with Ms. Angela

Talton, System Senior Vice President and Chief Diversity, Equity and Inclusion Officer at City of Hope, who now provides our application with a letter of support (attached).

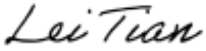
Should our current TRAN1 CIRM proposal be funded as hoped, and completed over 30 months, we will be in a position to continue Pre-IND and IND submissions and later to conduct a clinical trial for incurable pancreatic cancer with the novel engineered NK cell therapy. In the future trial, we will recruit all Californians regardless of racial, ethnic, gender and socioeconomic status to participate in the clinical trial. At that future time, we will utilize other resources at City of Hope as outlined in our revised 3-part section on DEI and in our responses to the constructive critique. Both documents are also attached to this cover letter.

One of us (MAC) has been an oncologist and physician-scientist for 35 years and has a strong record attending to the needs of underrepresented minority populations at both a local and national level (see revised DEI sections that are attached). While there is no cure for advanced pancreatic cancer, more underrepresented minorities (URMs) present with later stage disease and thus have a disproportionate share of this tragic burden. What is important about our therapy is that it is novel and thus far has been non-toxic. The production allows easy access to areas of need, i.e., the future clinical trial will not have to be conducted at City of Hope but as noted in our attached revisions, can be delivered in clinics that are in close proximity to the most underserved populations in California.

Currently, when a patient hears the three words: “you have cancer”, and the diagnosis is pancreatic cancer, no existing therapy offers hope of a prolonged survival. This diagnosis is equivalent to a death sentence. If funded, the preclinical work outlined in this TRAN1 CIRM proposal will bring us to the doorstep of a highly novel therapy for pancreatic cancer available to all Californians. We thus urge and appreciate the ICOC and CIRM administration to give strong consideration to fund our project in this funding cycle.

Thank you in advance for your consideration.

Sincerely,



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