City of Hope

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Independent Citizens Oversight Committee (ICOC)
California Institute for Regenerative Medicine (CIRM)
1999 Harrison Street, Suite 1650
Oakland, CA 94612

Application Number: CLIN1-11223
Title: CMV-specific T cells expressing anti-HIV CAR and CMV vaccine boost as immunotherapy for HIV/AIDS
Principal Investigator: Xiuli Wang, MD, PhD
GMP Manufacturing Lead: Angelo A. Cardoso, MD, PhD
Clinical Investigator: Elizabeth Budde, MD, PhD

Dear Chairman Thomas and Members of the ICOC:

We are delighted with the strongly positive review and unanimous recommendation from the Grants Working Group (GWG). Our approach, which they described as "*highly novel and based on sound scientific rationale*"…*"could eliminate the need for daily ART administration and could substantially improve patient outcome and quality of life".* It is estimated that only 55% of individuals with HIV achieved optimal adherence to antiretroviral therapy (ART) in the U.S., and ART has been associated with life-threatening drug toxicity. The GWG recognizes that our approach has the potential to be a single delivery therapy that releases patients from the ART regime for the rest of their lives. This strategy could also alleviate the cumulative financial burden that represents life-long medication.

While the GWG was highly enthusiastic, "*minor and addressable concerns*" were mentioned. We take this opportunity to address these below.

1. One concern was the use of an investigational CMV vaccine that is currently seeking FDA approval. First and foremost, we do not rely on an FDA approval of the CMV vaccine to test our therapeutic approach for HIV/AIDS in a Phase 1 clinical trial. The CMV vaccine developed at City of Hope has already been shown to be safe and immunogenic in 24 healthy volunteers [NCT01941056]. Based on this promising Phase 1 study, the CMV vaccine is now under evaluation in 102 bone marrow transplant recipients in a Phase 2 study [NCT02506933]. We are confident that the CMV vaccine will be able to safely expand our cell product.

2. Some reviewers noted that optimization for large-scale GMP manufacturing could delay the project. We have already performed 5 large-scale process development runs (3 with healthy donors and 2 with HIV-positive donors), with consistent outcomes, and have already secured a production slot at City of Hope for the lentiviral vector. We are, therefore, very confident that we will be able to complete the work as proposed.

In summary, we believe we have been thorough and realistic in planning this project, and are eager to develop our immunotherapy to help people living with HIV. Based on the expertise of our team and our interaction with the HIV community, we foresee no major hurdles to submitting an IND and initiating the clinical trial as soon as this project is completed.

Yours sincerely,

Xiuli Wang, MD, PhD