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June 12, 2020

Sub: Plan for Outreach to Underserved Communities- CIRM Application TRAN1COVID19-11975

Dear ICOC Chairman,

We thank the CIRM Grants Review Working Group for recommending our translational award application titled "COVID-19 Antiviral Therapy to Block Direct Cell Injury and Associated Tissue Damage". CIRM's support to this promising anti-viral drug molecule targeting COVID-19 would greatly accelerate its translational path to clinics.

Drug Candidate, dose selection and route of administration: This candidate drug, Berzosertib, is already in Phase 2 clinical investigation for cancer ailments and successful completion of the proposed study would quickly allow us to evaluate in COVID19 patients. The drug manufacturer is greatly excited by the new application of this compound and is supporting this study by providing clinical grade compounds and expertise to file for IND, dose selection and future clinical trials. Based on previous clinical trials, drug doses ranging from 140 mg/m2 to 210 mg/m2 were evaluated through intravenous (IV) route in cancer patients, which provided health benefits without any adverse events. For murine study, preclinical toxicological testing indicated that intravenous administration of Berzosertib at 10mg/kg, 20mg/kg and 60 mg/kg doses were well tolerated. We will evaluate 60 mg/kg dose, IV route, daily for 7 to 14 days after SARS-CoV-2 infection of human ACE2 transgenic mouse. Moreover, IC50 of Berzosertib identified in human stem cell derived lung organoids and ALI culture, which will be used for defining doses. The dosing details of previous Phase 1 and 2 studies from drug manufacture will be used to further refine the therapeutic dose and if needed dose escalation study design will be incorporated.

Clinical Investigator: The grant should position the project so that it will be ready for a pre-IND meeting with the FDA and ultimately initiation of a clinical trial. UCLA physician clinical trialist Dr. Otto Yang will serve as clinical investigator of the Phase1/2 clinical trial and in this role will join our team in the creation of the required materials for an FDA pre-IND meeting and ultimately an IND submission, including the clinical protocol. Dr. Yang has a strong track record of conducting COVID-19 clinical trials at UCLA.

Patient Diversity and Inclusion: Our COVID-19 clinical trials will be designed and ultimately delivered to a diverse population, especially those in underserved communities that have been disproportionately affected. UCLA's proven track record of success in investigator initiated clinical trials resulted in an $8M CIRM award to create the UCLA-UC Irvine Alpha Stem Cell Clinic (ASCC). We will have access to the ASCC which was established as a first-of-its-kind, cross-institutional "Center of Excellence" to overcome pre-clinical roadblocks and conduct clinical trials. The UCLA-UCI ASCC attracts a diverse patient base in Los Angeles and Orange counties that together constitute about 34% of the total California population and 12% of the total U.S. population. The outreach of UCLA-UCI ASCC and UCLA's satellite clinics throughout the greater Los Angeles area will allow for specifically reaching underserved populations that are most impacted by COVID-19 and translate the therapeutic benefit to the communities in the most need.

It is important to note that UCLA Health is among the most comprehensive and advanced healthcare systems in the world. More than 1,000,000 patients are seen annually in the UCLA Health outpatient facilities. It claims the largest university-based outpatient primary- and specialty-care system in the UC system. UCLA Health and UCI Health are two of the largest juxtaposed Accountable Care Organizations (ACOs) in the U.S. The combined UCLA and UCI ACOs cover southern California from Ventura to San Diego Counties. UCI Health includes 10 hospitals and more than 200 care sites in Orange County and southern Los Angeles County. Together the UCLA and UCI ACOs currently cover more than 3,000,000 lives.

We greatly appreciate the CIRM for supporting this important lifesaving study.

Yours sincerely,

Vaithi Arumugaswami