eFFECTOR and Quantitative Biosciences Institute (QBI) at UCSF Receive $5.0 Million from DARPA to Evaluate Zotatifin in COVID-19

May 4, 2021

Funding will support planned Phase 1b anti-viral study in patients with mild to moderate COVID-19 infections

SAN DIEGO, May 4, 2021 – eFFECTOR Therapeutics, Inc., a leader in the development of selective translation regulator inhibitors (STRIs) for the treatment of cancer, today announced a $5.0 million cooperative agreement sponsored by the Defense Advanced Research Projects Agency (DARPA) and the Defense Health Agency (DHA) to fund a planned Phase 1b study of zotatifin (eFT226) as an anti-viral agent in an outpatient setting for those with mild to moderate COVID-19 disease. The agreement is a subaward of a DARPA research program awarded to the Quantitative Biosciences Institute (QBI) at University of California, San Francisco (UCSF), headed by Brian Shoichet, Ph.D., professor, department of pharmaceutical chemistry, to identify agents active against SARS-CoV-2 infections. eFFECTOR's efforts will support the Phase 1b clinical study of zotatifin in patients with COVID-19 and related drug development activities.

Zotatifin is an investigational small molecule inhibitor of eukaryotic initiation factor 4A (eIF4A), an enzyme that unwinds complex RNA structures important to producing key disease-driving proteins. SARS-CoV-2 is an RNA virus that hijacks the human cellular machinery—including eIF4A—to replicate. Research led by Nevan Krogan, Ph.D., director of QBI, and the QBI Coronavirus Research Group (QCRG) at UCSF, identified host factor vulnerabilities of SARS-CoV-2 replication published in *Nature* in April 2020. This research demonstrated that zotatifin was one of the most effective agents in blocking viral replication of SARS-CoV-2 out of 69 compounds evaluated.

"This research agreement allows us to evaluate zotatifin's antiviral therapeutic potential in non-hospitalized patients suffering from mild to moderate SARS-CoV-2 infections," said Steve Worland, Ph.D., president and CEO of eFFECTOR. "Zotatifin may have broad utility against a number of coronaviruses, as *in vitro* studies have demonstrated that it is a potent inhibitor of SARS-CoV-2 and other coronavirus strains, including MERS-CoV."

Davide Ruggero, Ph.D., professor at the UCSF Helen Diller Cancer Center; an American Cancer Society Research Professor; and co-founder of eFFECTOR, added, "The interdisciplinary approach taken to establish zotatifin's *in vitro* activity against SARS-CoV-2, which included proteomics to identify interactions between host and viral proteins and recognition of clinical-stage drug candidates that impacted the identified pathway, exemplifies the broad collaborative efforts taken by QCRG scientists around the world in response to COVID-19."

About Zotatifin (eFT226)
Zotatifin is a potent and sequence-selective inhibitor of eukaryotic translation initiation factor 4A (eIF4A) mediated translation. eIF4A is responsible for unwinding complex structures in the non-coding 5' untranslated region of messenger RNA. Zotatifin is designed to inhibit the translation of mRNAs encoding several important oncogenes and survival factors, including receptor tyrosine kinases (RTKs), KRAS, Cyclin D, CDK4/6, and MYC. In vivo studies have shown potent in vivo tumor regression in multiple tumor models dependent on these factors, including non-small cell lung cancer and breast cancer. Since zotatifin inhibits the translation of mRNA in the non-coding region of mRNAs, it is not limited to any KRAS activating mutation subtypes. Zotatifin is currently being evaluated as an intravenous (IV) infusion in a Phase 1/2 clinical trial in patients with solid tumors.

Zotatifin will also be evaluated in a Phase 1b clinical trial in patients with mild to moderate COVID-19 infections pursuant to this grant sponsored by DARPA.

Please visit www.propelcovidclinicaltrial.com or www.clinicaltrials.gov for further information on ongoing clinical studies of zotatifin.

About QBI

The Quantitative Biosciences Institute (QBI) fosters collaborations across the biomedical and the physical sciences, seeking quantitative methods to address pressing problems in biology and biomedicine. Motivated by problems of human disease, QBI is committed to investigating fundamental biological mechanisms, because ultimately solutions to many diseases have been revealed by unexpected discoveries in the basic sciences. Learn more at qbi.ucsf.edu.

About UCSF

The University of California, San Francisco (UCSF) is exclusively focused on the health sciences and is dedicated to promoting health worldwide through advanced biomedical research, graduate-level education in the life sciences and health professions, and excellence in patient care. It includes UCSF Health, which comprises three top-ranked hospitals, as well as affiliations throughout the Bay Area. Learn more at https://www.ucsf.edu.

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About eFFECTOR

eFFECTOR is a next-generation oncology company developing a new class of targeted therapies called selective translation regulator inhibitors (STRIs). Tomivosertib, eFFECTOR's MNK1/2 inhibitor is being investigated in KICKSTART, a randomized, double-blind Phase 2 trial in non-small cell lung cancer (NSCLC) in combination with pembrolizumab. Zotatifin, eFFECTOR's inhibitor of eIF4A, is in a dose-escalation Phase 1 trial, with expansion cohorts expected to open in 2021. eFFECTOR has a global partnership with Pfizer developing inhibitors of eIF4E.

Contacts:

Investors:

Amy Conrad
Juniper Point
858-366-3243
amy@juniper-point.com

Media:

Heidi Chokeir, Ph.D.
Canale Communications
619-203-5391
heidi.chokeir@canalecomm.com