eFFECTOR Therapeutics Doses First Patient in Second Cohort of Phase 1b Clinical Trial of Zotatifin for the Treatment of COVID-19

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- Dose escalation based on positive recommendation from independent data safety monitoring board after safety review of cohort 1 -

- Drug levels achieved with sub-cutaneous formulation equivalent to IV formulation -

SAN DIEGO and REDWOOD CITY, Calif., Sept. 14, 2022 (GLOBE NEWSWIRE) -- eFFECTOR Therapeutics, Inc. (NASDAQ: EFTR), a leader in the development of selective translation regulator inhibitors ("STRIs") for the treatment of cancer, today announced it has dosed the first patient in the second cohort of its Phase 1b clinical trial of zotatifin in non-hospitalized adults with confirmed COVID-19 infection. The study is a double-blind, randomized, placebo-controlled trial evaluating the safety and antiviral activity of a single dose of zotatifin and is being conducted in collaboration with the Quantitative Biosciences Institute (QBI) at the University of California, San Francisco, under a $5 million cooperative agreement sponsored by the Defense Advanced Research Projects Agency.

Dose escalation to the second cohort comes after the positive recommendation of the independent data safety monitoring board upon review of safety data from the first dose cohort. The completed cohort also included the first subjects dosed with a sub-cutaneous formulation of zotatifin and preliminary analysis demonstrated equivalent plasma drug levels compared to IV delivery.

"As much as we all want to move past the COVID-19 pandemic, the virus has continued to evolve and there remains a need for well tolerated and effective antiviral medicines that can be easily accessed by vulnerable populations to prevent severe disease, hospitalization and death," said Steve Worland, Ph.D., president and chief executive officer of eFFECTOR. "Administered as a single dose injection, zotatifin aligns with the Test to Treat initiative being promoted by the U.S. government and has the potential to overcome many of the limitations of existing treatment options, including poor treatment adherence that can result in viral rebound. Achieving equivalent drug levels when zotatifin was delivered by the sub-cutaneous route provides an opportunity for convenient dosing in both the COVID and cancer settings."

Zotatifin is a potent and sequence-selective small molecule inhibitor of eIF4A, a host protein required to unwind the complex secondary structures within the 5' untranslated region of the genome of SARS-CoV-2 and other RNA viruses. Inhibiting the activity of eIF4A prevents the translation of the viral polyprotein needed for replication of the virus. Zotatifin was identified as a potent anti-SARS-CoV-2 agent in a study conducted by the international research consortium QBI Coronavirus Research Group (QCRG), led by Nevan Krogan, and previously published in *Nature*.

Zotatifin is a host-directed investigational therapeutic, meaning that it acts on a human protein that the SARS-CoV-2 virus hijacks to synthesize new viruses. As such, zotatifin may have a higher barrier to viral mutational escape than therapies that target components of the virus itself.

"If clinical results continue to demonstrate what we have observed in preclinical studies, zotatifin could have utility both in the treatment of COVID-19 – and diseases caused by other coronaviruses – as a monotherapy or in combination with other medicines," continued Dr. Worland. "It has the added potential to be an important tool in the arsenal for future pandemic preparedness."

About Zotatifin

Zotatifin is a potent and sequence-selective small molecule inhibitor of eIF4A that is designed to suppress expression of a network of cancer driving proteins, including Cyclins D and E, CDKs 2, 4 and 6 and select RTKs as well as KRAS. We are currently investigating zotatifin in ongoing clinical trials for solid tumors and, in collaboration with the University of California, San Francisco, as a potential host-directed antiviral therapy in patients with mild to moderate COVID-19.

About eFFECTOR Therapeutics

eFFECTOR is a clinical-stage biopharmaceutical company pioneering the development of a new class of oncology drugs referred to as STRIs. eFFECTOR's STRI product candidates target the eIF4F complex and its activating kinase, mitogen-activated protein kinase interacting kinase (MNK). The eIF4F complex is a central node where two of the most frequently mutated signaling pathways in cancer, the PI3K-AKT and RAS-MEK pathways, converge to activate the translation of select mRNA into proteins that are frequent culprits in key disease-driving processes. Each of eFFECTOR's product candidates is designed to act on a single protein that drives the expression of a network of functionally related proteins, including oncoproteins and immunosuppressive proteins in T cells, that together control tumor growth, survival and immune evasion. eFFECTOR's lead product candidate, tomivosertib, is a MNK inhibitor currently being evaluated in KICKSTART, a randomized, double-blind, placebo-controlled Phase 2b trial of tomivosertib in combination with pembrolizumab in patients with metastatic non-small cell lung cancer (NSCLC). Zotatifin, eFFECTOR's inhibitor of eIF4A, is currently being evaluated in Phase 2a expansion cohorts in certain biomarker-positive solid tumors, including ER+ breast cancer and KRAS-mutant NSCLC. eFFECTOR has a global collaboration with Pfizer to develop inhibitors of a third target, eIF4E. In addition to the company's oncology focus, zotatifin is being evaluated as a potential host-directed anti-viral therapy in patients with mild to moderate COVID-19 in collaboration with the University of California, San Francisco, under a $5 million cooperative agreement sponsored by the Defense Advanced Research Projects Agency.

About the Quantitative Biosciences Institute (QBI)

The Quantitative Biosciences Institute (QBI) is a University of California organized research unit reporting through the UCSF School of Pharmacy. 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.

Forward-Looking Statements

eFFECTOR cautions you that statements contained in this press release regarding matters that are not historical facts are forward-looking statements. The forward-looking statements are based on our current beliefs and expectations and include, but are not limited to, statements regarding: the potential of zotatifin as a treatment for COVID-19, diseases caused by other coronaviruses and in oncology; expectations of the COVID-19 market opportunity; and the potential therapeutic benefits of our other product candidates. Actual results may differ from those set forth in this press release due to the risks and uncertainties inherent in our business, including, without limitation: interim results of a clinical trial are not necessarily indicative of final results and one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data and as more patient data become available; potential delays in the commencement, enrollment and completion of clinical trials; additional disruptions to our operations from the COVID-19 pandemic, including clinical trial and manufacturing delays; our dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the results of preclinical studies and early clinical trials are not necessarily predictive of future results; the success of our clinical trials and preclinical studies for our product candidates is uncertain; we may use our capital resources sooner than expected and they may be insufficient to allow clinical trial readouts; regulatory developments in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval and/or commercialization, or may result in recalls or product liability claims; our ability to obtain and maintain intellectual property protection for our product candidates; and other risks described in our prior filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and we undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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