# eFFECTOR's Zotatifin Demonstrates in vitro Anti-SARS-CoV-2 Activity in Independent International Study Reported in Peer-Reviewed Journal Nature

**SAN DIEGO, April 30, 2020 (GLOBE NEWSWIRE)** — eFFECTOR Therapeutics, Inc., today announced that preliminary results from an independent preclinical study showed that oncology product candidate zotatifin (eFT226) had in vitro antiviral activity against SARS-CoV-2, the virus that causes COVID-19. The results of the research, led by Nevan Krogan, Ph.D., professor, department of cellular and molecular pharmacology and director of the Quantitative Bioscience Institute at UCSF, were reported today in the peer-reviewed journal Nature, in a manuscript titled "A SARS-CoV-2 Protein Interaction Map Reveals Host Targets for Drug-Repurposing" by David E. Gordon et al. Currently being tested in patients with solid tumors, zotatifin is a small molecule inhibitor of eukaryotic initiation factor 4A (eIF4A), an enzyme that unwinds complex RNA structures. SARS-CoV-2 is an RNA virus that hijacks the human cellular machinery—including eIF4A—to replicate.

"Antiviral activity is fully consistent with the mechanism of zotatifin, which is designed to inhibit an enzyme responsible for unwinding messenger RNA structures to enable the initiation of their translation into proteins, a process that viruses rely on to make their own proteins," said Steve Worland, Ph.D., president and chief executive officer of eFFECTOR. "This discovery underscores the importance of selective translation regulation inhibitors (STRIs), such as zotatifin, as a new class of product candidates, an area of expertise for eFFECTOR. While we remain focused on our cancer pipeline, we also now plan to explore zotatifin as a potential treatment for COVID-19 and look forward to finalizing those plans."

Zotatifin, which has demonstrated broad preclinical activity against multiple forms of KRAS mutant and receptor tyrosine kinase mutant cancers, is currently being evaluated in a Phase 1/2 clinical trial in patients with a targeted set of solid tumors [NCT04092673].

The experiments with zotatifin, conducted at Mount Sinai Hospital in New York and Institut Pasteur in Paris, were part of an international research effort, recently reported about in the New York Times, that seeks to accelerate the discovery and development of new drugs to treat patients with COVID-19 by evaluating compounds that were already being developed for other diseases. Scientists mapped the interactions that SARS-CoV-2 has with the host cell and then identified drugs that targeted those host proteins. The scientists procured and tested more than 69 compounds (29 FDA approved drugs, 12 drugs in clinical trials, including zotatifin, and 28 preclinical compounds) for their ability to inhibit SARS-CoV-2 in monkey cells. eFFECTOR's zotatifin was one of the most active agents identified in the study.

“The impressive data presented for zotatifin shows promise in blocking viral replication and could have significant implications for treating COVID-19 as well as infections caused by other RNA viruses that could drive a global pandemic,” said manuscript co-author, Kevan Shokat, Ph.D., professor and vice-chair, Department of Cellular and Molecular Pharmacology, UCSF; professor, Department of Chemistry, UC Berkeley; investigator, Howard Hughes Medical Institute; and co-founder of eFFECTOR. “RNA viruses have a high mutation rate, yet they all rely on human proteins to replicate, so a therapeutic strategy of targeting a human protein may have significant advantages for developing a drug that could overcome viral mutation and be stockpiled in the event of a future pandemic caused by an as yet unknown viral pathogen.”

Another co-author of the manuscript, Davide Ruggero, Ph.D., professor at the UCSF Helen Diller Cancer Center; an American Cancer Society Research Professor; and co-founder of eFFECTOR, who also participated in the international research effort, added, “The SARS-CoV-2 virus has evolved means for massive production of viral proteins in infected patients. The virus needs to usurp specific translation factors from the host cell to achieve this goal. If we can block the synthesis of these early proteins that the virus needs for its replication, this may have important therapeutic benefits in patients.”

Robert Sikorski, M.D., Ph.D., eFFECTOR’s chief medical officer, added, “If we can translate these striking scientific findings to a similar level of antiviral activity in patients, we believe there is potential for zotatifin early in the disease course to block virus replication before the onset of severe respiratory complications that can be fatal.”

Scientists unaffiliated with eFFECTOR continue to study zotatifin in the context of SARS-CoV-2. It is important to note that these are early studies not conducted in humans, and no evidence has yet been produced to demonstrate that zotatifin is an effective treatment for COVID-19 in patients.

Evaluating the therapeutic potential of zotatifin to combat COVID-19 requires submission of regulatory filings, clinical trials and manufacturing of sufficient quantities of the product candidate to support clinical testing, as well as the financing to support those activities. eFFECTOR is currently in contact with members of the biopharmaceutical and scientific communities, NIAID and funding sources to determine how to best advance zotatifin to potentially help combat the COVID-19 pandemic. eFFECTOR has already manufactured enough zotatifin to initiate clinical testing for COVID-19 while maintaining the pace of its initial, first-in-human, Phase 1/2 clinical trial in cancer patients that was initiated in November 2019.

**About Zotatifin**

Zotatifin is a potent and sequence-selective inhibitor of eukaryotic translation initiation factor 4A (eIF4A) mediated translation. Zotatifin is designed to inhibit the translation of mRNAs encoding several important oncogenes and survival factors, including several RTKS, KRAS, Cyclin D, CDK4/6, MYC, MCL1 and BCL-2, resulting in potent in vivo tumor regression in multiple tumor models dependent on these factors, including colorectal cancer, non-small cell lung cancer, breast cancer, hepatocellular carcinoma and B cell lymphomas. Since zotatifin

inhibits the translation of mRNA encoding KRAS and RTK, it is not limited to any mutation subtypes. The product candidate is currently being evaluated in a Phase 1/2 clinical trial in patients with solid tumors.

**About eFFECTOR Therapeutics**

eFFECTOR is a next-generation oncology company developing a new class of targeted therapies called selective translation regulator inhibitors (STRIs) that restore control of the processes that cancer cells manipulate for survival. The company's pipeline of product candidates target the cellular translation machinery that drive different, complementary systems cancer harnesses for growth and proliferation, creating the potential for combination use with each other or existing therapeutics. Tomivosertib, an inhibitor of MNK 1/2, works at multiple points in the cancer immunity cycle, and has demonstrated efficacy in a Phase 2 clinical trial in patients who progressed on checkpoint inhibitors. Zotatifin targets eIF4A, an enzyme responsible for unwinding complex RNA structures to facilitate transcription initiation. In preclinical studies, Zotatifin demonstrated broad activity against multiple types of KRAS mutant and receptor tyrosine kinase mutant tumors, and is being evaluated in an ongoing Phase 1 study in patients with solid tumors.

**Contacts:**

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

**Media:**
Heidi Chokeir, Ph.D.
Canale Communications
619-849-5377
heidi@canalecomm.com