eFFECTOR Therapeutics Reports Positive Interim Results in Zotatifin (eFT226) Phase 1/2 Clinical Trial at ASCO 2022 Showing Safety and Tolerability, and Initial Signals of Clinical Activity

June 5, 2022

Two partial responses observed in heavily pre-treated ER+ breast cancer patients

One ongoing cohort in ER+ breast cancer has been expanded and new expansion cohort planned in ER+ breast cancer patients with Cyclin D amplification

Management and key opinion leaders to present results and provide update on expanded development of zotatifin in investor call on June 5th at 7 p.m. ET / 6 p.m. CT

SAN DIEGO and REDWOOD CITY, Calif., June 05, 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 reported positive interim results of the company’s ongoing Phase 1/2 clinical trial of eIF4A inhibitor zotatifin in patients with solid tumors that showed treatment was generally well tolerated, resulted in suppression of multiple oncogenic drivers and demonstrated initial signals of clinical activity.

The interim data was presented today at the 2022 ASCO Annual Meeting in a poster, entitled “First-in-human phase 1/2 dose escalation and expansion study evaluating first-in-class eIF4A inhibitor zotatifin in patients with solid tumors,” by Funda Meric-Bernstam, M.D., chair of Investigational Cancer Therapeutics, and The Nellie B. Connally Chair in Breast Cancer at The University of Texas MD Anderson Cancer Center.

As of the cutoff date of March 4, 2022, interim results showed that zotatifin was generally well tolerated. Treatment emergent adverse events (TEAEs) related to zotatifin were mostly mild, readily managed and reversible, and included fatigue, anemia, diarrhea, vomiting and nausea. In the 25 patients who received the recommended Phase 2 dose, none exhibited zotatifin-related Grade 3, 4 or 5 TEAEs.

In Part 2 of the trial, early signals of clinical activity were observed in two patients with breast cancer. One patient with amplified Cyclin D1 and an ESR1 mutation, who had progressed on prior treatment with fulvestrant, experienced a confirmed partial response when zotatifin was combined with fulvestrant. A second partial response, which was awaiting confirmatory scan at the time of data analysis, was observed with the combination of zotatifin, fulvestrant and abemaciclib in a patient with PIK3CA mutations. Both patients were heavily pretreated for metastatic disease, having failed multiple lines of therapy prior to trial enrollment.

“The low emergence of adverse events with this entirely new class of medicines is a very important point to highlight,” said Dr. Meric-Bernstam. “Coupled with the initial signals of activity, these early results are encouraging for further development of zotatifin, especially in ER+ breast cancer.”

In a pharmacodynamic analysis measuring protein expression, modulation of protein translation by zotatifin was highly selective, with less than 1% of protein expression altered. Patients treated with zotatifin demonstrated reductions in the expression of key oncogenic drivers, including Cyclin E1 and Bcl-2. The most dramatic reductions in expression of these two proteins were seen in patients who showed the highest levels of expression prior to treatment with zotatifin.

“We are very encouraged by these interim data analyses as they provide evidence that zotatifin has the potential to suppress a network of cancer driving proteins and still remain generally well tolerated. Most cancers require suppression at multiple points in a complex network of cancer drivers to effectively manage disease. We saw encouraging results for down regulation of a number of oncogenic drivers, which not only provides clinical proof of mechanism, but also paves the way for how to combine zotatifin with other medicines,” said Steve Worland, Ph.D., president and chief executive officer of eFFECTOR. “Notably, based on the evidence, we have advanced to Stage 2 of a Simon 2-stage trial design in the cohort of patients treated with zotatifin and fulvestrant after progressing on a CDK4/6 inhibitor and endocrine therapy and plan to open a new cohort in patients with ER+ breast with Cyclin D1 amplification. We look forward to generating more data in this cohort as the resulting dataset in a defined patient population could support a potential path to registration. We anticipate reporting topline data from our current expansion cohorts by the end of 2022, as well as initial overall response rate data from the Cyclin D1 amplified ER+ breast cancer cohort in the first half of 2023.”

Based on zotatifin’s mechanism and results observed to date, the company has expanded the cohort evaluating zotatifin in combination with fulvestrant in ER+ breast cancer patients to 18 patients. A new cohort evaluating zotatifin in combination with fulvestrant in ER+ breast cancer patients with Cyclin D1 amplification is being planned.

Conference Call
eFFECTOR management will host a conference call with commentary from key opinion leaders to provide additional details of the interim study results and discuss upcoming milestones. Call details are as follows:

Date: June 5, 2022
Time: 7:00 p.m. ET | 6 p.m. CT | 4:00 p.m. PT
Conference ID: 7267595
Dial-in: Toll-Free Dial-In Number: (855) 493-1511; International Dial-In Number: (409) 497-0884

The webcast can be accessed on the “Events and Presentations” page of the “Investors” section of the Company’s website. The webcast will be archived and available for replay on the Company’s website for 30 days following the call. Please log on approximately 5 to 10 minutes prior to the

scheduled start time to download and install any audio software if needed. For more information, please visit investors.effector.com.

About the Phase 1/2 Trial
The open label study had enrolled a total of 54 patients with advanced solid tumors as of the cut off date of March 4, 2022 – 37 in the Phase 1 dose escalation portion and 17 in the Phase 2 expansion portion of the trial. The primary objectives of part one of the trial are to evaluate the safety and tolerability of zotatifin as a monotherapy in patients with defined, advanced solid tumors, determine the recommended Phase 2 dose for zotatifin as a monotherapy and to evaluate the PK profile. In part 2, the primary objective is to evaluate the preliminary antitumor activity of zotatifin as a monotherapy and as combination therapy in patients with defined, advanced solid tumors.

About Zotatifin (eFT226)
Zotatifin is a potent and sequence-selective small molecule inhibitor of eIF4A that is designed to supress 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 as a potential host-directed antiviral therapy in patients with mild to moderate COVID-19 in collaboration with the University of California, San Francisco.

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 grant sponsored by the Defense Advanced Research Projects Agency.

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: the future clinical development of our product candidates, including expectations on enrollment and the timing of reporting data from ongoing clinical trials; the planned expanded development of zotatifin and the timing thereof; and the potential therapeutic benefits of our 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 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; any future impacts to our business resulting from the conflict between Russia and Ukraine 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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