eFFECTOR Therapeutics Reports Positive Data Updates from Phase 2 Expansion Cohorts Evaluating Zotatifin in Patients with ER+ Metastatic Breast Cancer at the ASCO 2023 Annual Meeting

May 25, 2023

Partial responses observed in 5 of 19 (26%) evaluable patients treated with zotatifin 0.07 mg/kg combined with fulvestrant and abemaciclib (ZFA triplet) in heavily pretreated population
Partial response observed in 1 of 3 (33%) patients treated with zotatifin 0.1 mg/kg combined with fulvestrant (ZF doublet)
Both combinations were generally well tolerated with large majority of adverse events Grade 1 or 2
Company will host a virtual investor call on June 4, 2023, to discuss the data and clinical progress

SOLANA BEACH and REDWOOD CITY, Calif., May 25, 2023 (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 positive interim data updates from a Phase 2 expansion cohort evaluating zotatifin combined with fulvestrant and abemaciclib (ZFA triplet) in patients with ER+ metastatic breast cancer (mBC). These data, as well as initial data from further dose escalation, will be presented as a poster at the American Society of Clinical Oncology (ASCO) Annual Meeting, taking place June 2-6 in Chicago, IL by Ezra Rosen, M.D. from Memorial Sloan Kettering Cancer Center (MSK). The Company will host a virtual investor call on Sunday, June 4, 2023, at 6:30 PM CT / 7:30 PM ET to discuss the data and clinical progress. Sarat Chandarlapaty, M.D., Ph.D. of MSK will join the call to discuss the unmet medical need and current treatment landscape for patients with ER+ mBC.

"The activity observed with the ZFA triplet, with partial responses seen in 26% of patients, is substantially higher than we would expect for treating such heavily pretreated patients with just fulvestrant and abemaciclib," said Steve Worland, Ph.D., president and chief executive officer of eFFECTOR. "We believe this activity level reflects in part zotatifin's mechanism of down-regulating cyclins D and E, and the synergy this provides with CDK4/6 inhibition. The partial response observed at a higher dose of zotatifin in combination with only fulvestrant is encouraging and we look forward to reporting data from the completed dose escalation in the second half of 2023."

"I am excited about the early efficacy and safety results of the novel therapeutic candidate zotatifin and look forward to continuing its development in patients with advanced ER+ breast cancer who are currently medically underserved," added Doug Warner, M.D., chief medical officer of eFFECTOR.

New interim data were presented on the fully enrolled expansion cohort of patients (n=20) who received the ZFA triplet with zotatifin dosed at 0.07 mg/kg on Days 1 and 8 of 21-day cycles. Patients were heavily pre-treated, having received a median of four prior lines of therapy for metastatic disease. Five out of 19 (26%) RECIST-evaluable patients achieved a partial response (PR), including four confirmed and one unconfirmed. All five patients who achieved a PR had previously progressed on prior CDK4/6 and fulvestrant treatments, and all 5 had received one or more prior lines of chemotherapy. The disease control rate (DCR), reflecting patients with at least one on-treatment scan showing PR or stable disease (SD), was 14 of 19 (74%). PRs were seen in patients with and without mutations in the ESR1 and PIK3CA genes. As of the data cutoff date, 4 patients remained on therapy and progression free survival (PFS) as well as clinical benefit rate (CBR) data are not yet mature. The ZFA triplet was generally well tolerated, with 3 patients discontinuing due to adverse events (AEs) of any cause, and the large majority of AEs being Grade 1 or 2. The most frequent Grade 3 AEs were diarrhea in 3 of 20 (15%) patients, similar to the 13% frequency reported in the registrational Monarch 2 trial for abemaciclib and fulvestrant, and dyspnea in 2 of 20 (10%) patients.

New data were also reported for patients in resumed dose escalation cohorts utilizing the ZF doublet. In the one fully enrolled cohort, wherein patients received zotatifin dosed at 0.1 mg/kg every other week (Q2W) combined with fulvestrant, 1 of 3 (33%) patients achieved a PR on the first on-treatment scan, which was confirmed on the second on-treatment scan that occurred after the data cutoff, and remained on study. This patient had received four lines of prior therapy for metastatic disease, with progressive disease (PD) being the best overall response (BOR) to all four prior lines. Dose escalation is continuing at 0.14 mg/kg Q2W and 0.07 mg/kg once weekly (QW). Zotatifin has been generally well tolerated in dose escalation cohorts, with no dose limiting toxicities or serious adverse events observed.

Data for the ZF doublet with zotatifin at 0.07 mg/kg dosed on Days 1 and 8 of 21-day cycles, originally reported on January 5, 2023, were also updated. The patient with a confirmed PR showed a duration of response (DOR) of approximately 13 months. The patient with prolonged SD remained on study at 12 months.

Data on changes in circulating tumor DNA (ctDNA) were also updated from January 5, 2023, when the company reported a dose-dependent decrease in ctDNA in patients receiving zotatifin-based regimens. In the new data set, 9 patients who received the ZFA triplet at 0.07 mg/kg zotatifin had both pre- and on-treatment samples available for ctDNA analysis. Four additional patients came off study prior to the protocol-specified time to collect on-treatment ctDNA (Day 43). Eight patients had decreases in ctDNA of greater than 50%, representing 89% of the patients with on-treatment samples available for analysis, and 62% of patients who either had available on-treatment samples or who had discontinued prior to collection of on-treatment samples. The specific alleles observed to be decreased or eliminated in on-treatment ctDNA, including mutations in ESR1 and PIK3CA genes, reflect common mechanisms of resistance to endocrine therapy in ER+ BC and are consistent with zotatifin's mechanism of action maintaining sensitivity after resistance to endocrine therapy has emerged. The patient who achieved a confirmed PR in the ZF dose escalation group also eliminated detectable ctDNA at Day 29, including mutant alleles of ESR1 and ERBB2 genes, after having received only two doses of zotatifin.

All data was presented as of a data cut-off date of May 3, 2023.

MSK Disclosure: Dr. Chandarlapaty has financial interests related to eFFECTOR Therapeutics.

ASCO Presentation

Date: Sunday, June 4, 2023
Time: 8:00 to 11:00 a.m. CT
Abstract # 1080

Conference Call Information

eFFECTOR management will host a virtual investor call to discuss the data, clinical progress and featuring commentary from Sarat Chandarlapaty, M.D., Ph.D. of MSK on the unmet medical need and current treatment landscape for patients with ER+ metastatic BC. A live question and answer session will follow the formal presentations. To register for and attend the event, please click here.

Title: eFFECTOR Therapeutics Investor Event: Zotatifin in ER+ Metastatic Breast Cancer
Date: Sunday, June 4, 2023
Time: 7:30 p.m. ET/ 6:30 p.m. CT/4:30 p.m. PT

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: https://investors.effector.com/.

About the Phase 1/2 Trial

The Phase 1/2 trial (NCT04092673) is an open-label randomized dose-escalation and cohort-expansion study evaluating eIF4A inhibitor, zotatifin in patients with advanced solid tumors. 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

Zotatifin is a potent and sequence-selective small molecule inhibitor of the RNA helicase 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.

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.

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 therapeutic benefits of zotatifin, including based on its mechanism of action; and the future clinical development and data readouts of zotatifin and the timing thereof. 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 becomes available, including the risk that unconfirmed responses may not ultimately result in confirmed responses to treatment after follow-up evaluations; potential delays in the commencement, enrollment and completion of clinical trials; 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.

Contacts:

Investors:

Christopher M. Calabrese
Managing Director
LifeCam Advisors
917-680-5608
ccalabrese@lifesciadvisors.com

Kevin Gardner
Managing Director
LifeSci Advisors
617-283-2856
kgardner@lifesciadvisors.com

Media:

Mike Tattory
Account Supervisor
LifeSci Communications
609-802-6265
mtattory@lifescicomms.com