eFFECTOR Therapeutics Provides Positive Clinical Data Update for Zotatifin and General Corporate Update

January 5, 2023

Zotatifin continues to show favorable activity profile, including two confirmed partial responses (PR) among seven heavily pretreated subjects who received zotatifin, fulvestrant and abemaciclib (ECBF+A), with good tolerability

eFFECTOR to focus on front-line PD-L1 ≥ 50% cohort of KICKSTART trial with tomivosertib in non-small cell lung cancer

Management to present results and provide full pipeline update in investor call on January 5, 2023 at 4:30 p.m. ET

SOLANA BEACH, Calif. and REDWOOD CITY, Calif., Jan. 05, 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 provided an update on its ongoing clinical development programs for both zotatifin, in Phase 2 expansion cohorts for the treatment of estrogen receptor positive breast cancer (ER+ BC) and KRAS non-small cell lung cancer (KRAS NSCLC) as well as Phase 1 development for SARS-CoV-2 (COVID-19), and tomivosertib, in a Phase 2b trial for the treatment of non-small cell lung cancer (NSCLC) in combination with pembrolizumab, an established anti-immune checkpoint inhibitor used to treat various types of cancer.

“We are making steady headway across all our clinical programs and look forward to a number of key data milestones in 2023 for both the zotatifin and tomivosertib programs,” remarked Steve Worland, Ph.D., president and chief executive officer of eFFECTOR. “With zotatifin, we continue to see activity across both ER+ BC expansion cohorts, and the drug continues to be generally well-tolerated. The safety results to date have led us to believe that we may be able to increase the dose of zotatifin, which may achieve greater anti-tumor activity. Therefore, we have resumed dose escalation and plan to wait for dose escalation data as well as data from the ongoing ECBF+A cohort before pursuing additional expansion cohorts. We have also completed enrollment in the third and final cohort in our Phase 1b study with zotatifin in COVID-19 and anticipate providing top-line data from this trial in the first half of 2023.”

Zotatifin program update as of December 15, 2022:

- In the cohort (n=7) receiving zotatifin, fulvestrant and abemaciclib (ECBF+A), two patients experienced confirmed PRs, and a third patient had stable disease continuing beyond 24 weeks, for an objective response rate (ORR) of 29% (2/7) and a clinical benefit rate (CBR) of 43% (3/7). Zotatifin was generally safe and well-tolerated in this triplet combination. ORR and CBR data for the remaining 11 patients is anticipated to be available in the first half of 2023.
- In the ECBF cohort (n=18) receiving zotatifin and fulvestrant, one patient experienced a confirmed PR and one patient had stable disease continuing beyond 24 weeks. Zotatifin was generally safe and well-tolerated in this doublet combination.
- Dose-dependent target engagement was observed by two independent methods, without obvious signs of target saturation. Therefore, the company has resumed dose escalation with topline data anticipated in the second half of 2023.
- The company is deferring initiation of the Cyclin D1 amplified cohort in ER+ BC and pausing enrollment in the KRAS G12C lung cancer cohort until completion of dose escalation.
- Enrollment has completed in the third and final cohort in the Phase 1b COVID study.

“With regard to our tomivosertib program, clinical trial enrollment has been challenging across the entire industry and in particular in lung cancer, which impacted our KICKSTART trial,” continued Dr. Worland. “We believe that generating a strong signal indicating tomivosertib is an active agent is of the utmost importance for the program and for eFFECTOR at this juncture, and this could be accomplished through the readout of one randomized, placebo-controlled cohort. Therefore, we are focusing on completing enrollment in the PD-L1 ≥50% front-line cohort and are suspending further enrollment in the PD-L1 ≥1% maintenance cohort. We anticipate top-line results for the PD-L1 ≥50% front-line cohort in the second half of 2023.”

Tomivosertib Program Update:

- Enrollment challenges have persisted across both cohorts resulting from staffing issues across clinical sites and competition from other trials, and topline data from the frontline PD-L1$\geq$50% cohort is now anticipated to readout in the second half of 2023.
- The company is discontinuing further enrollment of the PD-L1$\geq$1% maintenance cohort.

“Overall, we are pleased with the progress we are making in our clinical programs, and we continue to act thoughtfully and deliberately to direct our attention and resources to where we believe clinical safety and efficacy can most quickly and effectively be demonstrated for both therapeutic candidates,” remarked Michael Byrnes, chief financial officer of eFFECTOR. “Concentrating our efforts selectively also allows us to manage our existing cash resources efficiently, which we believe will now carry us into the first quarter of 2024.”

Conference Call

eFFECTOR management will host a conference call to provide additional details and discuss upcoming milestones. Call details are as follows:

Date: January 5, 2023
Time: 4:30 p.m. ET | 3:30 p.m. CT | 1:30 p.m. PT
Webcast Registration URL:
https://onlinexperiences.com/Launch/QReg/ShowUUID=05FFAFE1-2C84-4055-8AC5-4F793B325365
Audio Conference Registration URL: https://register.vevent.com/register/BI6cdb48c163b348bc9876364f6295a6fb

The webcast can be accessed on the “Investors” section of eFFECTOR’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 scheduled start time to download and install any audio software if needed.

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 as a potential host-directed antiviral therapy in patients with mild to moderate COVID-19 in collaboration with UCSF.

About the Zotatifin Phase 1/2 Trial

The open label study had enrolled a total of 37 patients with advanced solid tumors in the Phase 1 dose escalation portion of the trial. In the expansion portion of the trial, a total of 18 patients with breast cancer were enrolled in the ECBF cohort, which evaluates zotatifin in combination with fulvestrant after progression on CDK treatment, and enrollment is ongoing in the ECBF+A cohort, which evaluates zotatifin in combination with fulvestrant and abemaciclib. 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 two, 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 Tomivosertib

Tomivosertib is eFFECTOR’s wholly-owned, highly selective translation regulation inhibitor that targets mitogen-activated protein kinase interacting kinase (MNK). The oral, small molecule drug candidate has been shown to enhance killing of tumor cells by T cells, delay T-cell exhaustion/dysfunction and enhance the T-cell central memory pool, in part by down-regulating multiple checkpoint proteins including PD-1, PD-L1, TIM-3 and LAG-3. Tomivosertib is being evaluated in KICKSTART, eFFECTOR’s randomized, double-blind, placebo-controlled Phase 2b study in NSCLC in combination with pembrolizumab. The KICKSTART trial builds on results obtained in an earlier study of tomivosertib as an extension of checkpoint inhibitor treatment in patients experiencing insufficient response to a U.S. Food and Drug Administration (FDA)-approved checkpoint inhibitor alone.

About the Tomivosertib Phase 2b KICKSTART trial in NSCLC

KICKSTART is a randomized, double-blind, placebo-controlled clinical trial assessing the efficacy and safety of tomivosertib in combination with pembrolizumab, an FDA-approved PD-1 inhibitor, as frontline combination therapy. Patients enrolled in this trial will have demonstrated biomarker expression of PD-L1 >50% assessed by an FDA-approved diagnostic test. These NSCLC patients are generally the most responsive patient population to immunotherapy and most often receive checkpoint inhibitors as a monotherapy as standard of care.

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, 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 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 antiviral therapy in patients with mild to moderate COVID-19 in collaboration with UCSF, which holds a $5 million cooperative agreement 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 update on expanded development of zotatifin and the timing thereof; the potential therapeutic benefits of our product candidates; the potential market opportunity for our product candidates; and our expected cash runway and the sufficiency of our capital resources to allow clinical trial data readouts and the expansion of our clinical development programs; and the potential to raise any capital under the LPC facility and the use of proceeds from any capital raised. 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: the risk that 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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