eFFECTOR Therapeutics Provides Pipeline and Business Updates

January 24, 2022

Tomivosertib development strategy updated, including addition of a new cohort in Phase 2b KICKSTART trial in non-small cell lung cancer (NSCLC) evaluating frontline maintenance in PD-L1 ≥1% patient population, representing additional $5 billion U.S. market opportunity

First patients dosed in two additional Phase 2 expansion cohorts evaluating zotatifin in combination with sotorasib in KRAS G12C-mutant NSCLC and in combination with abemaciclib and fulvestrant in ER+/HER2- breast cancer

Company enters into investment agreement with Lincoln Park Capital for up to $50 million

Management to host investor call January 24 at 5 p.m. ET

SAN DIEGO and REDWOOD CITY, Calif., Jan. 24, 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 multiple pipeline updates for its ongoing development programs, as well as the establishment of an investment agreement with Lincoln Park Capital for a commitment of up to $50 million over 36 months. In the randomized Phase 2b KICKSTART trial of tomivosertib in combination with pembrolizumab in NSCLC, a new cohort has been added to evaluate frontline maintenance in patients with PD-L1 ≥1%, an estimated $5 billion potential U.S. market opportunity. Additionally, the company is discontinuing development of tomivosertib in patients who have already progressed on pembrolizumab monotherapy. Topline data from the ongoing frontline cohort in patients with PD-L1≥50% and the new frontline maintenance cohort in patients with PD-L1≥1% in the KICKSTART trial are now expected in the first half 2023. Separately, in the Phase 2a trial evaluating zotatifin in patients with solid tumors, the company dosed patients in two new expansion cohorts.

"The prioritization of tomivosertib development in NSCLC to focus on treatment in virtually all PD-L1 positive patients nearly doubles the addressable patient population we are evaluating in our randomized Phase 2b KICKSTART trial, with a potential combined market opportunity of $9 billion," said Steve Worland, Ph.D., president and CEO of eFFECTOR. "Our decision to discontinue the frontline extension cohort of the KICKSTART trial was made to optimize our tomivosertib development strategy and not due to any safety or efficacy concerns. While there is continuing unmet medical need in patients with PD-L1≥50% who have progressed on pembrolizumab monotherapy, this market opportunity is much smaller than the opportunities presented by treating patients prior to progression across the PD-L1 positive landscape. Additionally, we anticipate the market opportunity to treat after progression will further diminish as frontline immuno-therapy combination regimens, potentially including tomivosertib, improve upon current patient outcomes achieved with checkpoint inhibitor monotherapy. The expansion of our second development program, zotatifin, into two additional high-need patient populations, capitalizes on zotatifin's potential to downregulate KRAS and the estrogen receptor, both of which drive cancer in these respective patient populations."

Premal Patel, M.D., chief medical officer of eFFECTOR, added, "The incorporation of immuno-therapy to the standard of care has significantly improved outcomes for NSCLC patients, yet many patients still do not respond and most patients who do respond will go on to develop resistance over time. The addition of agents such as tomivosertib, which are designed to activate T cells and delay or prevent their dysfunction, is a particularly exciting strategy to potentially enhance response to anti-PD-(L)1 therapies such as pembrolizumab."

Tomivosertib Update
Upon continued evaluation of the evolving treatment landscape, eFFECTOR has updated its portfolio strategy for tomivosertib to address a much broader patient population, significantly increasing the market potential for this product candidate.

eFFECTOR has updated the design of its double-blind, randomized Phase 2b KICKSTART trial of tomivosertib in NSCLC to include a new cohort, which will enroll patients with PD-L1 ≥1% who have initiated frontline therapy with pembrolizumab combined with platinum-based chemotherapy. This cohort will enroll approximately 60 patients with PD-L1 ≥1% NSCLC immediately after they complete the platinum chemotherapy phase (4-6 cycles) of their frontline treatment without disease progression. Patients in this cohort will be randomized 1:1 to standard-of-care maintenance therapy plus tomivosertib in the treatment group versus standard-of-care maintenance plus placebo in the control group. Standard-of-care maintenance therapy is defined as pembrolizumab + pemetrexed in non-squamous NSCLC and pembrolizumab in squamous NSCLC.

Enrollment continues in the frontline PD-L1 ≥50% cohort in the KICKSTART trial, which will evaluate approximately 60 patients, but has been slower than originally anticipated. Reasons for slow enrollment include the impact of COVID-19 on site operations and an evolving treatment landscape with greater than anticipated use of chemotherapy + pembrolizumab as frontline therapy. The company has taken multiple steps to drive enrollment, including increasing the number of trial sites and continuing emphasis on the importance of PD-L1 testing to select optimal frontline therapy, especially for patients with PD-L1 ≥50% who may be managed using a chemotherapy-free regimen. The company believes these mitigation efforts, combined with our patient and physician outreach activities, will enhance enrollment.

These two cohorts represent the large majority of advanced NSCLC patients and a significant market opportunity, estimated at $9 billion in the U.S. There are ~70,000 U.S. patients with metastatic, unresectable NSCLC with PD-L1 ≥1%. Of those patients, ~43,000 have PD-L1 status 1-49%, and standard frontline treatment is anti-PD-(L)1 therapy combined with chemotherapy. Approximately 80% of patients treated with this frontline treatment continue on anti-PD-(L)1 maintenance therapy following chemotherapy and would be candidates for tomivosertib in combination in the maintenance setting, representing an addressable population of ~34,000. In addition, there are ~27,000 patients with PD-L1 status ≥50% for whom single agent anti-PD-(L)1 therapy is an accepted standard as frontline therapy that would be candidates to receive tomivosertib in combination.

The company has discontinued enrollment in the frontline extension cohort of the KICKSTART trial, which was evaluating tomivosertib as an add-on to treatment in NSCLC patients who had progressed on pembrolizumab, representing the smallest NSCLC population of ~9,000 patients. Enrollment in this cohort had been slower than anticipated, in part due to reluctance of patients to continue pembrolizumab monotherapy treatment after progression in the control group. In addition, the treatment landscape is rapidly evolving for frontline NSCLC such that pembrolizumab monotherapy use may diminish in the future.

Across the two active cohorts the company plans to enroll approximately 120 patients randomized equally to receive standard-of-care plus tomivosertib versus standard-of-care plus placebo. Primary endpoints of the trial are progression free survival (PFS) in each cohort separately, with key secondary endpoints being safety, objective response rate (ORR) and overall survival (OS). Topline data readouts from both cohorts are now anticipated to occur in the first half of 2023.

Pending positive results from the KICKSTART Phase 2b clinical trial, the company plans to advance tomivosertib into Phase 3 registration trials. If results from the KICKSTART trial are clinically and statistically significant, the company plans to explore the potential for accelerated approval with the FDA.

Zotatifin Update
In the ongoing Phase 1/2 dose escalation and expansion trial of zotatifin in multiple solid tumors, patients have been dosed in two recently opened combination cohorts: KRAS G12C-mutant NSCLC in combination with sotorasib; and ER+/Her2- breast cancer in combination with fulvestrant and abemaciclib. Two additional breast cancer cohorts, ER+/FGFR+ evaluating zotatifin as monotherapy and ER+ evaluating zotatifin in combination with fulvestrant, continue to enroll.

The primary objective of this trial is to assess the safety, tolerability and activity of zotatifin as a monotherapy treatment and in combination with targeted agents in biomarker-specific patient populations. If positive activity is observed in one or more Phase 2a expansion cohorts, the company plans to evaluate zotatifin, potentially as a combination in a randomized trial against a relevant comparator control group, or potentially in a single-arm monotherapy trial following demonstration of an appropriate ORR in the Phase 2a monotherapy expansion cohort.

eFFECTOR anticipates reporting initial response data from one or more of the expansion cohorts, as well as additional data from the Phase 1 dose escalation portion of the trial, in the first half of 2022. The company anticipates reporting topline results from the trial in the second half of 2022.

Financial Update
eFFECTOR expects that its existing cash resources will allow it to read out initial response and topline results from the ongoing Phase 2a dose-expansion cohorts in the zotatifin program, as well as topline data from both of the active cohorts in the ongoing Phase 2b KICKSTART trial.

eFFECTOR has executed a purchase agreement with Lincoln Park Capital Fund, LLC (LPC). Under the terms of the agreement, eFFECTOR has the right to sell, at its discretion, up to $50 million of shares of the company's common stock to LPC over a 36-month period, subject to certain limitations and conditions set forth in the agreement. In consideration for entering into the agreement, eFFECTOR issued LPC shares of common stock as a commitment fee. Under the terms of the purchase agreement, an initial purchase of $3 million will be made after satisfaction of certain conditions, including the declaration of effectiveness of an S-1 registration statement, to be filed with the Securities and Exchange Commission (SEC). The company expects this commitment from Lincoln Park Capital will provide financial flexibility and is aligned with eFFECTOR's long-term strategy for value creation.

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

Date: January 24, 2022
Time: 5:00 p.m. ET | 2:00 p.m. PT
Conference ID: 6577617
Dial-in: Toll-Free Dial-In Number: (855) 493-1511; International Dial-In Number: (409) 497-0884

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 eFFECTOR Therapeutics
eFFECTOR is a clinical-stage biopharmaceutical company focused on 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 multiple 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 as a monotherapy and in combination with approved therapies 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.

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 potential future registrational trials and plans to potentially seek accelerated approval; the expected timing of reporting data from our clinical trials; the potential therapeutic benefits of our product candidates; the potential market opportunity for our product candidates; the sufficiency of our capital resources to allow clinical trial data readouts; and the timing and amount of any capital raised 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: 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 ability to access the LPC facility is subject to certain conditions, including the SEC must declare a registration statement on Form S-1 effective; 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 may be insufficient to allow clinical trial data 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; we may use our capital resources sooner than we expect; and other risks described in our prior filings with the SEC, including under the heading “Risk Factors” in our most recent quarterly report on Form 10-Q and any subsequent filings with the SEC. 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:
Stephanie Carrington
ICR Westwicke
646-277-1282
Stephanie.Carrington@westwicke.com

Media:
Heidi Chokeir, Ph.D.
Canale Communications
619-203-5391
heidi.chokeir@canalecomm.com