eFFECTOR Therapeutics Reports Fourth Quarter and Full Year 2023 Financial Results and Provides Corporate Update

March 25, 2024

Topline data from the randomized Phase 2b KICKSTART trial of tomivosertib combined with pembrolizumab in non-small cell lung cancer (NSCLC) expected in early April 2024

Median progression free survival (mPFS) of 7.4 months in the ZFA expansion cohort evaluating zotatifin in combination with fulvestrant and abemaciclib in heavily pretreated patients

Received U.S. FDA Fast Track designation for zotatifin in combination with fulvestrant and abemaciclib for treatment of ER+/HER2- advanced metastatic breast cancer

Raised $15.0 million in gross proceeds from registered direct financing, extending cash runway into first quarter of 2025

SOLANA BEACH, Calif. and REDWOOD CITY, Calif., March 25, 2024 (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 financial results for the fourth quarter and year ended December 31, 2023, and provided a corporate update.

“In 2023 we continued to advance the development of our two wholly-owned clinical assets, tomivosertib and zotatifin, while strengthening our balance sheet to extend cash runway into the first quarter of 2025,” remarked Steve Worland, Ph.D., president and chief executive officer of eFFECTOR. “We are excited to report topline results, expected in early April 2024, from our randomized, placebo-controlled Phase 2b KICKSTART trial of tomivosertib, an MNK inhibitor designed to activate T cells, combined with pembrolizumab in frontline metastatic NSCLC. These data will include progression-free survival (PFS), the primary endpoint of the trial, as well as select secondary endpoints. These results, if positive, would enable activities, including interactions with regulatory agencies, intended to support initiation of a Phase 3 registrational trial.”

“We are also pleased with the progress of zotatifin, including the 7.4 month mPFS previously reported for the ZFA expansion cohort that evaluated zotatifin in combination with fulvestrant and abemaciclib in heavily pretreated patients with ER+ breast cancer,” continued Dr. Worland. “In light of favorable safety and tolerability data, and in order to optimize zotatifin’s therapeutic potential, we resumed dose escalation using a more convenient schedule of dosing every other week. We look forward to finalizing the dose and schedule for zotatifin prior to interacting with the FDA in the second half of 2024, utilizing the recently granted Fast Track designation to expedite further development. We believe the zotatifin program is well positioned to move into a randomized trial in late 2024.”

Pipeline Highlights

Tomivosertib (eFT508): eFFECTOR’s wholly-owned, highly selective MNK inhibitor designed to enhance anti-tumor immune activity by activating T cells, delaying their exhaustion, and expanding the pool of central memory T cells:

- **Topline results from Phase 2b KICKSTART trial in NSCLC expected in early April 2024.** The company expects the release of topline data in early April, which will reflect a database snapshot taken on March 19, 2024, will include the primary endpoint of PFS and secondary endpoints including safety, Objective Response Rate (ORR), and an initial analysis of Overall Survival (OS). More mature OS data is anticipated in the second half of 2024. The primary analysis will reflect 37 PFS events, which provides approximately 80% power to detect a PFS hazard ratio of 0.65 at a p≤0.2. The KICKSTART trial enrolled 54 patients with PD-L1 expression ≥50% who were randomized to receive tomivosertib or placebo, in combination with pembrolizumab, as their initial therapy for metastatic disease. If positive results are obtained from KICKSTART, we plan to interact with the FDA in the second half of 2024 prior to initiating a Phase 3 registration trial.
- **Phase 1 investigator-initiated dose escalation trial in patients with relapsed/refractory Acute Myeloid Leukemia (AML) in collaboration with Northwestern University.** Currently enrolling patients, the trial is designed to capitalize on previously published results that showed preclinical activity of tomivosertib in AML models. Once the appropriate dose for tomivosertib in AML is identified, the company hopes to expand the trial to test tomivosertib in combination with venetoclax and azacytidine. The study is led by Shira Dinner, M.D., Associate Professor of Medicine (Hematology and Oncology) at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Zotatifin (eFT226): eFFECTOR’s wholly-owned potent and selective inhibitor of mRNA helicase eIF4A designed to downregulate expression of key oncoproteins and cell cycle proteins that drive tumor growth and resistance:

- **Positive interim Phase 2 data including mPFS of 7.4 months in the ZFA triplet expansion cohort reported at the 2023 San Antonio Breast Cancer Symposium (SABCS®).** In the ZFA triplet cohort, wherein patients with a median of

four prior lines of therapy for metastatic disease received 0.07 mg/kg zotatifin dosed on Days 1 and 8 of a 21-day cycle, combined with fulvestrant and abemaciclib, the mPFS was 7.4 months (95% confidence intervals 2.8 to non-estimable). As previously reported, five of 19 (26%) RECIST-evaluable patients had partial responses, including four confirmed and one unconfirmed. The ZFA triplet continued to be generally well tolerated, with the majority of zotatifin-related treatment-emergent adverse events (TEAEs) being Grade 1 or 2. The most common zotatifin-related TEAEs were nausea, vomiting, and fatigue, all of which were Grade 1 or 2. The most common Grade 3 or higher zotatifin-related TEAEs were anemia and blood creatinine phosphokinase increase, each in two of 20 (10%) patients. Four of 20 (20%) of patients discontinued treatment due to adverse events of any cause.

- **Dose escalation now focused on the ZFA triplet.** Based on favorable safety and tolerability results observed in more than 50 patients who received zotatifin at the initial recommended Phase 2 dose (RP2D) of 0.07 mg/kg on Days 1 and 8 of a 21-day cycle, as monotherapy, ZF doublet or ZFA triplet, dose escalation was resumed using a more convenient schedule of zotatifin dosed every other week (Q2W). In the first quarter of 2024, dose escalation of the ZF doublet concluded with the determination of 0.2 mg/kg zotatifin Q2W as the new RP2D for the doublet, which is projected to provide approximately twice the overall zotatifin exposure compared to the initial RP2D. Determination of the RP2D for the ZFA triplet is ongoing. The company looks forward to finalizing the dose and schedule for zotatifin in the ZFA triplet and interacting with the FDA prior to initiating a randomized, potentially registrational, trial in ER+ breast cancer.

- **Ongoing patient enrollment in investigator-initiated randomized Phase 2 study in ER+ breast cancer.** The study is being conducted as part of a collaboration with Stanford Medicine in which zotatifin is being tested in specific genomically-defined subgroups, including standard-risk patients as well as high-risk patients carrying specific markers predictive of relapse. The trial is led by Jennifer Caswell-Jin, M.D., Assistant Professor of Medicine at Stanford Medicine, and brings to the clinic the science of integrative subgroups of breast cancer, building on work done by Christian Curtis, Ph.D., Professor of Medicine, Genetics, and Biomedical Data Science, and Director of Artificial Intelligence and Cancer Genomics at Stanford Medicine.

Business Highlights

- **$15.0 million in gross proceeds raised from registered direct financing, extending cash runway into the first quarter of 2025.** The Company completed a registered direct financing that closed on January 29, 2024, which included the sale of an aggregate of 1,488,834 shares of common stock (or common stock equivalents in lieu thereof), at a purchase price of $10.075 per share (or common stock equivalent in lieu thereof) and warrants to purchase up to an aggregate of 1,488,834 shares of common stock with an exercise price of $9.95 per share.

Fourth Quarter and Full Year 2023 Financial Results

Cash Position and Guidance: The company had cash, cash equivalents, and short-term investments totaling $18.4 million as of December 31, 2023, compared to $26.3 million as of December 31, 2022. After incorporating the net proceeds of $13.6 million raised from the registered direct financing in January 2024, the company anticipates that its cash, cash equivalents, and short-term investments will be sufficient to fund operations into the first quarter of 2025.

Revenue: Revenue was zero for the quarter ended December 31, 2023, compared to approximately $0.7 million for the same quarter of 2022. Revenue for the full year of 2023 was zero, compared to $3.6 million for the full year of 2022. Revenue for the year ended December 31, 2022, consisted of grant revenue in connection with the company's subaward from the University of California San Francisco under a grant from DARPA to investigate new COVID-19 treatments.

Research and Development (R&D) Expenses: R&D expenses were $6.1 million for the quarter ended December 31, 2023, compared to $6.6 million for the same quarter of 2022. R&D expenses were $22.9 million for the year ended December 31, 2023, compared to $23.3 million for the year ended December 31, 2022. This decrease for the year was due to lower consultant and personnel costs, along with lower external development expenses surrounding the zotatifin program, partially offset by increased external development expenses surrounding the KICKSTART trial for tomivosertib. R&D expenses included approximately $1.9 million and $2.6 million of non-cash stock compensation expense in the years ended December 31, 2023, and 2022, respectively.

General and Administrative (G&A) Expenses: G&A expenses were $2.5 million for the quarter ended December 31, 2023, compared to $2.7 million for the same quarter of 2022. G&A expenses were $10.9 million for the year ended December 31, 2023, compared to $12.6 million for the year ended December 31, 2022. This decrease for the year was primarily due to a decrease in the cost of director and officer insurance premiums, reduced personnel-related costs, and reduced professional service costs, including external audit and legal. G&A expenses included approximately $2.6 million and $2.7 million of non-cash stock compensation expense in the years ended December 31, 2023, and 2022, respectively.

Other Income (Expense): Other expense was $0.5 million for the quarter ended December 31, 2023, and 2022. Other expense was $2.0 million for the year ended December 31, 2023, and other income was $9.7 million for the year ended December 31, 2022. Other expense in the year ended December 31, 2023, consisted primarily of interest expense associated with the company's term loans. Other income in the year ended December 31, 2022, consisted primarily of income related to the change in fair value of the company's earn-out liability for the period, partially offset by interest expense associated with the company's term loans. The fair value of the share earn-out liability of $61.0 million at the closing date of the business combination in August 2021 was remeasured at $6 thousand as of December 31, 2022. The earn-out period expired in August 2023 resulting in a reduction of the corresponding earn-out liability to zero as of December 31, 2023.

Net Loss: Net loss was $9.1 million, or $3.42 per basic and diluted share, for the quarter ended December 31, 2023, as compared to $9.3 million, or $5.57 per basic and diluted share, for the same quarter of 2022. Net loss was $35.8 million, or $16.37 per basic and diluted share, for the year ended December 31, 2023, as compared to $22.7 million, or $13.76 per basic and diluted share, for the year ended December 31, 2022. Shares outstanding as of December 31, 3023, and 2022 were 2,982,679 and 1,667,602, respectively, after taking into effect the retroactive application of the 25:1 reverse stock split completed on January 12, 2024.

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 designed to activate T cells and is currently being evaluated in KICKSTART, a randomized, double-blind, placebo-controlled Phase 2b trial of tomivosertib in combination with pembrolizumab as frontline treatment 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: the future clinical development of our product candidates, including expectations on enrollment and the timing of reporting data from ongoing clinical trials and Phase 3 registrational programs; the potential therapeutic benefits of our product candidates, including potential lines of therapy and in multiple patient segments; and the sufficiency of our capital resources to fund operations into the first quarter of 2025. 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, data readouts 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; any future impacts to our business resulting from inflation or other geopolitical developments outside our control; 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.

eFFECTOR Therapeutics, Inc.
Condensed Consolidated Balance Sheets
(in thousands)

	December 31, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 14,875	$ 8,708
Short-term investments	3,495	17,602
Prepaid expenses and other current assets	1,468	1,704
Total current assets	19,838	28,014
Property and equipment, net	140	241
Operating lease right-of-use assets	53	111
Other assets	513	711
Total assets	$ 20,544	$ 29,077
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 2,330	$ 1,486
Accrued expenses	2,921	3,368
Current term loans, net	19,385	19,061
Accrued final payment on term loans, current	1,100	1,100
Lease liabilities, current portion	60	60
Total current liabilities	25,796	25,075
Other accrued liabilities, non-current	503	—
Earn-out liability	—	6
Non-current warrant liability	40	40

Non-current lease liabilities	—	60
Total liabilities	26,339	25,181
Stockholders' equity (deficit):		
Preferred stock	—	—
Common stock	—	—
Additional paid-in capital	173,582	147,480
Accumulated other comprehensive loss	—	(18)
Accumulated deficit	(179,377)	(143,566)
Total stockholders' equity (deficit)	(5,795)	3,896
Total liabilities and stockholders' equity (deficit)	$ 20,544	$ 29,077

eFFECTOR Therapeutics, Inc.
Condensed Consolidated Statement of Operations and Comprehensive loss
(Unaudited)
(in thousands, except share and per share data)

	Three Months Ended December 31,		Year Ended December 31,	
	2023	2022	2023	2022
	(Unaudited)			
Grant revenue	$ —	$ 674	$ —	$ 3,553
Operating expenses:				
Research and development	6,073	6,649	22,919	23,313
General and administrative	2,524	2,748	10,925	12,643
Total operating expenses	8,597	9,397	33,844	35,956
Operating loss	(8,597)	(8,723)	(33,844)	(32,403)
Other income (expense)	(532)	(538)	(1,967)	9,738
Net loss	(9,129)	(9,261)	(35,811)	(22,665)
Other comprehensive income (loss)	1	51	18	(18)
Comprehensive loss	$ (9,128)	$ (9,210)	$ (35,793)	$ (22,683)
Net loss per share, basic and diluted	$ (3.42)	$ (5.57)	$ (16.37)	$ (13.76)
Weighted-average common shares outstanding, basic and diluted [1]	2,669,960	1,662,871	2,186,954	1,647,183

(1) Shares outstanding have been retroactively adjusted to reflect the 25:1 reverse split that occurred on January 12, 2024.

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