eFFECTOR Therapeutics to Collaborate with Stanford Medicine on Investigator-Initiated Randomized Phase 2 Study in Patients with ER+ Breast Cancer

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The Company's eIF4A inhibitor, zotatifin, will be tested in specific genomically-defined subgroups, including standard risk patients as well as high-risk patients carrying specific markers predictive of relapse

SOLANA BEACH, Calif. and REDWOOD CITY, Calif., April 11, 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 a clinical collaboration with Jennifer Caswell-Jin, M.D., Assistant Professor of Medicine at Stanford Medicine, who will serve as principal investigator in an investigator-initiated trial evaluating zotatifin in patients with estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer in a pre-operative setting. This trial will bring to the clinic the science of integrative subgroups of breast cancer, building on work done by Christina Curtis, Ph.D., Professor of Medicine, Genetics, and Biomedical Data Science, and Director of Artificial Intelligence and Cancer Genomics at Stanford Medicine.

"ER+ breast cancer carries a significant, long-term risk of distant relapse, which is further increased in patients with high-risk genomic profiles," said Dr. Caswell-Jin. "Professor Curtis and her colleagues previously identified eight subtypes of ER+ breast cancer, four of which are at high risk of distant relapse[1]. Two of these high-risk subtypes present an increase in genes encoding the proteins that zotatifin has been demonstrated to selectively downregulate in preclinical studies. This clinical trial will investigate how zotatifin might affect tumor growth, compared to standard of care, in patients with these specific high-risk genomic profiles, as well as in patients with standard risk. The goal is to develop precision approaches to improve breast cancer outcomes."

"This investigator-led study presents a unique opportunity to complement eFFECTOR's existing development strategy with cutting-edge expertise in next-generation genomic predictive technologies to continue exploring the clinical potential of zotatifin for treating breast cancer," said Doug Warner, M.D., chief medical officer of eFFECTOR Therapeutics. "These efforts complement eFFECTOR's growing body of evidence of zotatifin's activity in metastatic ER+ breast cancer. Our aim in the Stanford collaboration is to explore the potential to improve early targeted cancer therapy with zotatifin, to potentially delay or prevent future relapse. This approach is in contrast to a single genetic marker to predict an immediate response to therapy. Current targeted therapies fail too many patients, and we hope this collaboration will help identify better treatment regimens with improved clinical benefit for patients."

Dr. Curtis and Dr. Caswell-Jin's research applies genomic data to define specific subgroups of breast cancer that predict higher risk of relapse after treatment with endocrine therapy, with or without chemotherapy. These subgroups at high risk of relapse are identified through analysis of molecular data from approximately 2,000 breast cancer patients with up to 20 years of clinical follow-up. To identify therapies that might provide clinical benefit to these particularly high-risk patients, Dr. Caswell-Jin will direct an umbrella, randomized pre-operative trial testing integrative subtype-targeted therapeutics in ER+/HER2- breast cancer. Zotatifin will be investigated in a cohort of patients at high risk of relapse, including a group with overexpression of cyclin D1 and fibroblast growth factor 3, proteins that promote cancer growth and survival, and a separate group with overexpression of fibroblast growth factor receptor 1, as well as in a cohort of patients at standard risk for relapse. In both cohorts, patients will be randomized to receive a single dose of zotatifin plus fulvestrant, or fulvestrant alone, 14 days before surgery. The primary objective of the study is to assess change in tumor proliferative status, as measured by Ki67 staining, from baseline to 14 days after preoperative treatment with either regimen.

[1] https://www.nature.com/articles/s41586-019-1007-8

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.

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: the clinical development of zotatifin; the potential benefits of the collaboration; and the potential therapeutic benefits of zotatifin. 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: we are dependent on Stanford to conduct the investigator-initiated clinical program; potential delays in the commencement, enrollment and completion of clinical trials; the success of our clinical trials and preclinical studies for our product candidates is uncertain; the inability to realize any benefits from the collaboration; 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; 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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