

**Prospectus Supplement No. 1
(To Prospectus dated April 2, 2024)**

eFFECTOR Therapeutics, Inc.



This prospectus supplement updates, amends and supplements the prospectus dated April 2, 2024 (the "Prospectus"), which forms a part of our Registration Statement on Form S-1 (Registration No. 333-262339). Capitalized terms used in this prospectus supplement and not otherwise defined herein have the meanings specified in the Prospectus.

This prospectus supplement is being filed to update, amend and supplement the information included in the Prospectus with the information contained in our Current Report on Form 8-K (the "Current Report"), filed with the SEC on April 4, 2024. Accordingly, we have attached the Current Report to this prospectus supplement.

This prospectus supplement is not complete without the Prospectus. This prospectus supplement should be read in conjunction with the Prospectus, which is to be delivered with this prospectus supplement, and is qualified by reference thereto, except to the extent that the information in this prospectus supplement updates or supersedes the information contained in the Prospectus.

Our common stock and warrants are listed on the Nasdaq Capital Market under the symbols "EFTR" and "EFTRW." On April 3, 2024, the closing price of our common stock was \$16.47 and the closing price of our warrants was \$0.14.

We are an "emerging growth company" under federal securities laws and are subject to reduced public company reporting requirements. Investing in our securities involves certain risks. See "Risk Factors" beginning on page 10 of the Prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if the Prospectus or this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is April 4, 2024.

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): April 4, 2024

eFFECTOR Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-39866
(Commission
File Number)

85-3306396
(I.R.S. Employer
Identification No.)

142 North Cedros Avenue, Suite B
Solana Beach, California
(Address of principal executive offices)

92075
(Zip Code)

(858) 925-8215
(Registrant's telephone number, including area code)
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, \$0.0001 par value per share	EFTR	Nasdaq Capital Market
Warrants to purchase common stock	EFTRW	Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (Sec.230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (Sec.240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On April 4, 2024, eFFECTOR Therapeutics, Inc. (the “Company”) announced topline results from the primary analysis of the randomized Phase 2 KICKSTART trial which tested tomivosertib or placebo, each combined with pembrolizumab, as frontline treatment for patients with non-small cell lung cancer (“NSCLC”) with PD-L1 $\geq 50\%$. Based on 36 events, the hazard ratio for progression free survival (“PFS,” the primary endpoint of the study) using a stratified Cox proportional hazards model was 0.62 (95% confidence intervals 0.3 to 1.3) in favor of tomivosertib. The two-sided p value for PFS, based on a stratified log rank test, was 0.21, which did not meet the pre-specified threshold of $p \leq 0.2$. The median PFS was 13.0 weeks in the tomivosertib plus pembrolizumab arm and 11.7 weeks in the placebo plus pembrolizumab arm, respectively. Overall survival results remain immature, however no trend favoring tomivosertib was observed. There were 67% Grade 3 or higher treatment emergent adverse events in the tomivosertib plus pembrolizumab arm versus 37% in the placebo plus pembrolizumab arm.

While there was evidence of modest tomivosertib activity in the trial, based on the totality of the data currently available the Company does not see an obvious path forward to continue developing tomivosertib in frontline NSCLC. The Company plans to focus its development efforts on advancing zotatifin, which has a novel mechanism distinct from that of tomivosertib and is targeted to enter a randomized, potentially registrational trial in estrogen receptor positive (“ER+”) breast cancer later this year. The Company is focused on advancing zotatifin through development as efficiently as possible, building on the recent positive updates of median PFS (“mPFS”) and safety data at last year’s San Antonio Breast Cancer Symposium. As a next step for the zotatifin program, the Company expects to report additional data, including the recommended Phase 2 dose (“RP2D”), for zotatifin combined with fulvestrant and abemaciclib in the second half of 2024. In addition, as part of the Company’s strategy to leverage investigator-sponsored trials to conserve capital, a separate, investigator-sponsored trial of tomivosertib in acute myeloid leukemia (“AML”) will continue unchanged. The Company’s mechanistic rationale to test tomivosertib in AML is entirely distinct from the rationale in NSCLC and relies on tomivosertib’s potential to inhibit production of survival proteins Mcl-1 and Bcl-2, which are required for leukemia cell survival.

Forward-Looking Statements

The Company cautions you that statements contained in this report regarding matters that are not historical facts are forward-looking statements. The forward-looking statements are based on the Company’s current beliefs and expectations and include, but are not limited to: the potential therapeutic benefits of its product candidates; the Company’s plans to focus its development efforts on, and advance the development of, zotatifin in ER+ breast cancer, including the potential for additional data, determination of an RP2D and to enter a registrational trial, the timing thereof; the Company’s expectations for the continuation of the investigator initiated study of tomivosertib in AML; the Company’s strategy to maximize the value of all assets in its pipeline; and its plans regarding the presentation of data findings at a future medical conference. Actual results may differ from those set forth in this report due to the risks and uncertainties inherent in the Company’s business, including, without limitation: interim results previously reported for the zotatifin 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; topline results that the Company reports is based on a preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the clinical trial and such topline data may not accurately reflect the complete results of a clinical trial; the Company may be unable to identify a path forward for zotatifin or tomivosertib based on its limited capital resources, which the Company may use sooner than expected and may be insufficient to allow clinical trial readouts or further clinical development or for the Company to continue its operations; the Company’s lender may seek to declare a default under its loan and security agreement to the extent that a material adverse change in the Company’s business is deemed to have occurred or otherwise accelerate immediate repayment of all outstanding obligations under its loan agreement; its 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 the Company’s clinical trials and preclinical studies for its product candidates is uncertain; regulatory developments in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of the Company’s 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 the Company’s 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 the Company undertakes 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.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: April 4, 2024

eFFECTOR Therapeutics, Inc.

By: /s/ Michael Byrnes
Name: Michael Byrnes
Title: Chief Financial Officer