

**Prospectus Supplement No. 15
(To Prospectus dated March 21, 2022)**

eFFECTOR Therapeutics, Inc.



This prospectus supplement updates, amends and supplements the prospectus dated March 21, 2022 (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 February 21, 2023. 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 February 17, 2023, the closing price of our common stock was \$0.61 and the closing price of our warrants was \$0.17.

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 7 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 February 21, 2023.

**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): February 21, 2023

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 February 21, 2023, eFFECTOR Therapeutics, Inc. (the “Company” or “eFFECTOR”) announced top-line results from its Phase 1b clinical trial of zotatifin for the treatment of COVID demonstrating favorable safety results as well as positive trends in several measures of antiviral activity. The Company also presented preclinical data that demonstrated the breadth of zotatifin’s activity against RNA viruses. These results were presented at the 30th Conference on Retroviruses and Opportunistic Infections on February 20, 2023.

The primary objective of the trial was to evaluate safety of zotatifin in subjects with mild-to-moderate COVID. Zotatifin was generally well tolerated at all doses, with injection site reactions from the sub-cutaneous route (all Grade 1 or 2) being the only adverse event showing a potential relationship to zotatifin dose. Secondary and exploratory objectives included evaluation of antiviral activity in nasal and saliva samples and pharmacokinetics (“PK”). Trends in antiviral activity favoring zotatifin over placebo were seen by several assessments. In particular, in saliva, which was sampled more frequently than nasal cavity, virus level undetectability (“VLU”) was achieved approximately twice as fast in the zotatifin-treated subjects compared to placebo, with a median time to VLU of three days for zotatifin in comparison to seven days for placebo. The Hazard Ratio (“HR”) for achieving VLU in saliva was 2.83 (95% confidence intervals 0.64, 12.5; $p=0.13$) in favor of zotatifin. Zotatifin administered by the sub-cutaneous route showed very similar PK parameters compared to IV administration in other trials, supporting continued development of zotatifin by the sub-cutaneous route. The half-life of zotatifin was measured to be approximately 4 days (across all dosing groups), supporting further development of zotatifin as a single administration to treat COVID.

In the randomized, double-blind, placebo-controlled dose escalation trial, 27 subjects received zotatifin at doses ranging from 0.01 to 0.035 mg/kg and nine subjects received placebo. At the outset of the trial, one patient received zotatifin and one patient received placebo by intravenous administration. All other subjects ($n=34$) received study drug by sub-cutaneous injection. Enrolled subjects had mild or moderate COVID and were positive for SARS-CoV-2 RNA or antigen within 7 days of randomization. The trial was conducted in collaboration with the Quantitative Biosciences Institute (“QBI”) at the University of California, San Francisco (“UCSF”), which holds a \$5 million cooperative agreement sponsored by the Defense Advanced Research Projects Agency.

The Company also presented results from preclinical studies in which zotatifin was active against numerous COVID isolates and other coronaviruses and was 10-100 times more potent, than several agents authorized by the U.S. Food and Drug Administration for treatment of COVID, based on concentrations required to achieve comparable reductions in virus yield and protection from virus-induced cytopathic effects in cell-based assays.

Forward-Looking Statements

eFFECTOR cautions you that statements contained in this current report 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, statements regarding: the future clinical development of zotatifin the potential of zotatifin as a treatment for COVID, diseases caused by other coronaviruses and in oncology; expectations of the COVID market opportunity; and the potential therapeutic benefits of our product candidates. Actual results may differ from those set forth in this current report 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 as more patient data becomes available; potential delays in the commencement, enrollment and completion of clinical trials; additional disruptions to our operations from the COVID 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; 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.

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: February 21, 2023

eFFECTOR Therapeutics, Inc.

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