

Prospectus Supplement No. 9
(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. 333-259751). 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 June 6, 2022. 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 June 3, 2022, the closing price of our common stock was \$1.79 and the closing price of our warrants was \$0.20.

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 6 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 June 6, 2022.

**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): June 5, 2022

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 June 5, 2022, eFFECTOR Therapeutics, Inc. (the “Company” or “our”) reported positive interim results of the Company’s ongoing Phase 1/2 clinical trial of zotatifin that showed treatment was generally well tolerated, resulted in suppression of multiple oncogenic drivers and demonstrated initial signals of clinical activity. The interim data was presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting.

As of the cutoff date of March 4, 2022, interim results showed that zotatifin was generally well tolerated. Treatment emergent adverse events (“TEAEs”) related to zotatifin were mostly mild or moderate, and included fatigue, anemia, diarrhea, vomiting and nausea. In the 25 patients who received the recommended Phase 2 dose, none exhibited zotatifin-related Grade 3, 4 or 5 TEAEs.

In Part 2 of the trial, early signals of clinical activity were observed in two patients with breast cancer. One patient with amplified Cyclin D1 and an ESR1 mutation, who had progressed on prior treatment with fulvestrant, experienced a confirmed partial response when zotatifin was combined with fulvestrant. A second partial response, which was awaiting confirmatory scan at the time of data analysis, was observed with the combination of zotatifin, fulvestrant and abemaciclib in a patient with PIK3CA mutations. Both patients were heavily pretreated for metastatic disease, having failed multiple lines of therapy prior to trial enrollment.

In a pharmacodynamic analysis measuring protein expression, modulation of protein translation by zotatifin was highly selective, with less than 1% of protein expression altered. Patients treated with zotatifin demonstrated reductions in the expression of key oncogenic drivers, including Cyclin E1 and Bcl-2. The most dramatic reductions in expression of these two proteins were seen in patients who showed the highest levels of expression prior to treatment with zotatifin.

In addition, the Company has advanced to Stage 2 of a Simon 2-stage trial design in the cohort of patients treated with zotatifin and fulvestrant after progressing on a CDK4/6 inhibitor and endocrine therapy and plans to open a new cohort in patients with ER+ breast with Cyclin D1 amplification. The Company plans to generate more data in this cohort as the resulting dataset in a defined patient population could support a potential path to registration. The Company anticipates reporting topline data from its current expansion cohorts by the end of 2022, as well as initial overall response rate data from the Cyclin D1 amplified ER+ breast cancer cohort in the first half of 2023.

Based on zotatifin’s mechanism and results observed to date, the Company has expanded the cohort evaluating zotatifin in combination with fulvestrant in ER+ breast cancer patients to 18 patients. A new cohort evaluating zotatifin in combination with fulvestrant in ER+ breast cancer patients with Cyclin D1 amplification is being planned.

The open label study had enrolled a total of 54 patients with advanced solid tumors as of the cutoff date of March 4, 2022 – 37 in the Phase 1 dose escalation portion and 17 in the Phase 2 expansion portion of the trial. The primary objectives of part one of the trial are to evaluate the safety and tolerability of zotatifin as a monotherapy in patients with defined, advanced solid tumors, determine the recommended Phase 2 dose for zotatifin as a monotherapy and to evaluate the PK profile. In part 2, the primary objective is to evaluate the preliminary antitumor activity of zotatifin as a monotherapy and as combination therapy in patients with defined, advanced solid tumors.

Forward-Looking Statements

The Company 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: expectations on enrollment and the timing of reporting data from ongoing clinical trials; the future clinical development of our product candidates, including the planned expanded development of zotatifin and the timing thereof; and the potential therapeutic benefits of our product candidates. 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 and completion of clinical trials; additional disruptions to our operations from the COVID-19 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; 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 press releases and filings with the Securities and Exchange Commission (“SEC”), including under the heading “Risk Factors” in the our annual report on Form 10-K 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.

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.

eFFECTOR Therapeutics, Inc.

Date: June 6, 2022

By: /s/ Michael Bynes

Name: Michael Bynes

Title: Chief Financial Officer