Prospectus Supplement No. 12 (To Prospectus dated March 16, 2023)

eFFECTOR Therapeutics, Inc.



This prospectus supplement updates, amends and supplements the prospectus dated March 16, 2023 (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 November 28, 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 November 27, 2023, the closing price of our common stock was \$0.5731 and the closing price of our warrants was \$0.1166.

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 November 28, 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): November 28, 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. \Box

Item 8.01 Other Events.

On November 28, 2023, eFFECTOR Therapeutics, Inc. (the "Company") announced that the U.S. Food and Drug Administration ("FDA") has granted Fast Track designation for zotatifin in combination with fulvestrant and abemaciclib ("ZFA triplet") as second- or third-line therapy for the treatment of adult patients with estrogen receptor-positive, human epidermal growth factor-negative advanced or metastatic breast cancer with disease progression following treatment with endocrine therapy and a CDK 4/6 inhibitor. The Fast Track designation was granted following FDA review of preclinical and clinical data for zotatifin, including recent safety and efficacy data for the ZFA triplet.

Fast Track designation is available to a product if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. This designation is intended to facilitate development and expedite review of drugs to treat serious and life-threatening conditions so that an approved product may reach the market expeditiously.

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 our current beliefs and expectations and include, but are not limited to: the future clinical development of our product candidates; the potential therapeutic benefits of our product candidates; and our ability to realize the benefits from zotatifin receiving Fast track designation from the FDA. Actual results may differ from those set forth in this report due to the risks and uncertainties inherent in our business, including, without limitation: Fast Track designation may not result in a more expedited development or regulatory review process, and such a designation does not increase the likelihood that zotatifin will receive marketing approval in the United States; Fast Track designation does not change the standards for regulatory approval; the FDA may later decide that zotatifin no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened; 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; 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 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.

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.

By: /s/ Michael Byrnes

Name: Michael Byrnes Title: Chief Financial Officer

Date: November 28, 2023