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): October 26, 2021

CORTEXYME, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-38890**	**90-1024039**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

269 East Grand Ave. **South San Francisco, California** **(Address of principal executive offices)**	**94080** **(Zip Code)**

Registrant's telephone number, including area code: (415) 910-5717

Not Applicable
(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 240.13d-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, par value $0.001 per share	**CRTX**	**Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§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 October 26, 2021, Cortexyme, Inc. (the "Company") reported top-line results from its Phase 2/3 GAIN Trial, a double-blind, placebo-controlled study evaluating the efficacy of atuzaginstat (COR388), an investigational orally administered small-molecule that targets gingipain proteases from the bacterium Porphyromonas gingivalis (P. gingivalis). The 643-participant study in mild to moderate patients with Alzheimer's disease did not meet statistical significance in its co-primary cognitive and functional endpoints as measured by ADAS-Cog11 and ADCS-ADL at end of the treatment period in the overall cohort.

The pre-specified subgroup of participants with P. gingivalis DNA detectable in saliva at baseline (PG-DS; n=242) showed a dose response, with a 57% slowing of cognitive decline as measured by ADAS-Cog11 in the 80 mg BID arm (p=0.02) and a 42% slowing in the 40 mg BID arm (p=0.07) vs. placebo. Significant benefits in this subgroup were not seen on the other co-primary, ADCS-ADL. The cognitive benefit of atuzaginstat in patients with high P. gingivalis infection was reinforced by similar results in multiple pre-specified infection related subgroups and with multiple methods of analysis. Additionally, reductions in P. gingivalis in saliva at week 24 were significantly correlated with improved outcomes at the end of the treatment period as measured by ADAS-Cog11 (p=0.0007), Clinical Dementia Rating–Sum of Boxes (CDR) (p=0.004), Mini-Mental State Exam (MMSE) (p=0.007), and a beneficial trend on ADCS-ADL (p=0.08).

The sub-study in periodontal disease demonstrated a trend to benefit on the primary clinical endpoint of pocket depth in the same pre-specified sub-group with P. gingivalis DNA detectable in saliva. Further results will inform the next stage of development in periodontitis and will be presented at a future scientific conference.

Most adverse events were mild to moderate in severity. The most common were gastrointestinal, such as diarrhea in up to 16% and nausea in 6% of participants treated with atuzaginstat vs. 3% and 2% of placebo participants, respectively. Atuzaginstat was associated with dose-related liver enzyme elevations >3X the upper limit of normal: 2% on placebo, 7% on 40 mg BID, and 15% on 80 mg BID. These elevations alone were not clinically significant, and virtually all participants were asymptomatic. Two participants in the 80 mg BID arm had concomitant bilirubin elevations without alternative explanation. Lab changes resolved while participants remained on drug or after withdrawal without any known long-term adverse effects. Atuzaginstat treated groups showed no increase in ARIA (amyloid-related imaging abnormalities), including microhemorrhage and edema, or superficial siderosis.

In light of the GAIN Trial results and the significant unmet medical need in Alzheimer's, the Company is actively engaging with regulators, the medical community, patient advocacy groups, and other key stakeholders to advance development of atuzaginstat and the second-generation lysine-gingipain inhibitor COR588, which is differentiated by novel compound properties and once daily administration.

Forward-Looking Statements.

Statements in this Current Report on Form 8-K contain "forward-looking statements" that are subject to substantial risks and uncertainties. Forward-looking statements contained in this Current Report on Form 8-K may be identified by the use of words such as "anticipate," "expect," "believe," "will," "may," "should," "estimate," "project," "outlook," "forecast," "potential" or other similar words. Examples of forward-looking statements include, among others, plans to present additional data from the GAIN Trial at CTAD 2021 and other medical meetings, the strategic development path for atuzaginstat, its business plans, strategy, planned clinical trials and timeline, prospects, and milestone expectations; the timing and success of the Company's clinical trials and related data, including with respect to the GAIN Trial, as well as enabling and human studies of COR588; the potential of atuzaginstat to treat Alzheimer's disease, periodontal disease, and other potential indications; the timing of announcements and updates relating to its clinical trials and related data; the potential therapeutic benefits, safety and efficacy of the Company's product candidate or library of compounds and statements about its ability to obtain, and the timing relating to, further development of atuzaginstat and COR588, regulatory submissions and related response and decisions, including with respect to the Company's partial clinical hold, and approvals with respect to the Company's drug product candidate. For such statements, the Company claims the protection of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are based on the Company's current expectations and are subject to inherent uncertainties, risks, and assumptions that are difficult to predict and could

cause actual results to differ materially from what the Company expects. Further, certain forward-looking statements are based on assumptions as to future events that may not prove to be accurate. Factors that could cause actual results to differ include, but are not limited to, the risks and uncertainties described in the section titled “Risk Factors” in the Company’s Annual Report on Form 10-K filed with the Securities and Exchange Commission (the “SEC”) on March 1, 2021, its Quarterly Report on Form 10-Q filed with the SEC on August 6, 2021, and other reports as filed with the SEC. Forward-looking statements contained in this Current Report on Form 8-K are made as of this date, and the Company undertakes no duty to update such information except as required under applicable law.

SIGNATURES

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.

CORTEXYME, INC.

By: /s/ Caryn G. McDowell

Date: October 26, 2021 Title: Chief Legal and Administrative Officer and Corporate Secretary