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

DIVISION OF
CORPORATION FINANCE

April 2, 2019

Casey C. Lynch
Chief Executive Officer
Cortexyme, Inc.
269 East Grand Ave.
South San Francisco, CA 94080

Re: Cortexyme, Inc.
Draft Registration Statement on Form S-1
Submitted March 4, 2019
CIK No. 0001662774

Dear Ms. Lynch:

We have reviewed your draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

Draft Registration Statement on Form S-1

Prospectus Summary, page 1

1. We refer to the first paragraph of your Summary, which highlights that Alzheimer's patients treated with COR388 showed "positive trends of improvement" across "several" exploratory cognitive tests commonly used in Alzheimer's trials. Please revise your Summary here and on page 2 to balance your presentation concerning the significance of the efficacy results demonstrated from testing nine patients. In this regard, we note that your CEO's October 24-27 presentation, concluded, "There was a trend of improvement in some of the cognitive tests...; however, these results should be interpreted with caution

due to the small sample size." In addition, we note that your disclosure on page 94 indicates that two of the three conducted tests did not produce statistically significant results.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies and Significant Judgments and Estimates
Stock-Based Compensation
Common Stock Valuations, page 74

2. Once you have an estimated offering price or range, please explain to us how you determined the fair value of the common stock underlying your equity issuances and the reasons for any differences between the recent valuations of your common stock leading up to the IPO and the estimated offering price. This information will help facilitate our review of your accounting for equity issuances including stock compensation and beneficial conversion features.

Results of Operations
Research and Development Expenses, page 76

3. Please revise the disclosure to disaggregate research and development expenses by nature or type of expense for each period presented.

Business, page 83

4. Given the large number of preclinical tests discussed or referenced in your prospectus, please consider whether a table briefly identifying these studies and their purpose would assist investors in understanding your preclinical work and statements, including those concerning:
   - the presence of *P. gingavalis* in the brain;
   - the causal link between *P. gingavalis* and Alzheimer's; and
   - successful treatment of Alzheimer's disease pathology with gingipain inhibitors, including with your COR388 inhibitor.

5. Please revise to discuss in greater detail the following preclinical testing:
   - the human observational study showing that 100% of 50 mild to moderate Alzheimer's patients tested positive using your proprietary test for *P. gingivalis* DNA fragments in cerebral spinal fluid (CSF) (pages 2 and 89) and
   - your detection of the presence of *P. gingavalis* DNA from multiple genes, confirming the presence of bacteria (page 89).

6. At first use, please describe the following terms employed concerning your testing results:
   - "demonstrated effects";
   - "positive trends of improvement";
   - "clinically significant trends";
   - "clinically meaningful changes"; and
   - "numerical trends of improvement".

   Also, revise your discussions of testing results, where necessary for context, to present p-values and to clarify whether the results are or are not statistically significant. For instance, we note your discussions on pages 94-95 concerning MMSE and CANTAB results do not provide p-values or address statistical significance.

7. We note your disclosures on pages 89 and 93 indicating that you have developed proprietary technology to test for the presence of *P. gingavalis* DNA fragments in the CSF. Please tell us, and revise, as applicable, to discuss whether there are challenges or uncertainties with respect to testing for the presence of *P. gingavalis* in the human brain.

P. gingivalis and the Role of Gingipains, page 88

8. Please reconcile your disclosure on page 88, which appears to attribute the work to your collaborators at the University of Auckland, and the second sentence of the prospectus summary, which highlights "your seminal discovery" observed across multiple studies to date. Please note that we may have additional comment after reviewing your response.

P. gingivalis Infection Causes Alzheimer's Disease Pathology in Mice, page 89

9. We note your statement indicating that the ability to reproduce disease in an infected animal is an important criterion for demonstrating causation. Please revise to identify briefly other criteria typically used to demonstrate causation, or advise.

10. We refer to your disclosure on page 1 highlighting that you have "observed that *P. gingavalis* infection causes Alzheimer's pathology in animal models." We note; however, that your discussion under the heading on page 89 appears limited to discussion of a single animal model. In revising this section, please be sure to identify and explain the work that your team conducted. Also, identify any other studies or factors that form the basis for your conclusions concerning causation.

Exploratory Cognitive Testing, page 94

11. We note your disclosure on page 2 and elsewhere noting that the study was not "designed to be powered for significance" on cognitive tests. Accordingly, please tell us, and revise the discussion of your cognitive testing on Alzheimer's patients, as applicable, to explain the implications of conducting testing and presenting efficacy results where the study was not designed to be powered for significance. With reference to your disclosure on page 100 concerning the IND and IRB processes, please tell us whether this exploratory testing was conducted pursuant to an FDA-authorized IND and whether you submitted the testing protocols to FDA. Similarly, please tell us whether an IRB reviewed and approved the study plan and protocols.

12. Please explain why you chose to test using three measures (MMSE, CANTAB, WLA) but did not test using ADAS-Cog 11. In this regard, we refer to your disclosure on page 1 that ADAS-Cog 11 has served as a key endpoint in supporting regulatory approval of drugs for Alzheimer's disease as well as your disclosure on page 95 that you have selected mean change in ADAS-Cog 11 as the primary endpoint for your planned Phase 2/3 GAIN clinical trial.

13. Please revise your discussion of each of the three measures (MMSE, CANTAB, WLA) to explain the results in Figure 7 and to demonstrate the numerical trend of improvements or statistically significant improvement cited.

14. Please revise your discussion of the Winterlight speech-based cognitive assessment (WLA) to address the following:
    - Revise to present the endpoints and results for each of the three WLA measurements that you highlight. Here, we note that Figure 7 appears to depict results for only one measurement, or possibly a portion thereof (*i.e.*, use of prepositions).
    - Indicate whether WLA analysis was limited to the three measurements you present.
    - Discuss whether FDA has accepted WLA testing as the basis for review and/or approval of drugs for Alzheimer's treatment or any drugs treating other diseases, disorders or conditions that impact cognitive function. Here, we note your risk factor disclosure on page 11.

Our Planned Phase 2/3 GAIN Clinical Trial of COR388, page 95

15. We note that your discussion on page 102 concerning human clinical studies in support of an NDA indicates that Phase 2 and Phase 3 are typically conducted in sequential phases. Please revise to discuss your decision to combine these two phases, including any attendant challenges. Also, revise to discuss the current regulatory status of the proposed GAIN trial. In this regard, your disclosure on page 11 suggests that FDA acceptance of your GAIN trial remains pending.

Intellectual Property, page 98

16. Please revise your disclosure regarding your intellectual property to clarify the jurisdiction in which you hold issued patents and pending applications.

17. We refer to your disclosure on page F-25 concerning a research grant and license agreement with an unidentified stockholder. Please revise your intellectual property section to add disclosure concerning this agreement. Identify the counterparty, discuss the subject of the license, and clarify whether the $1.05 million is an annual limitation. Also, file the agreement as an Exhibit to the registration statement or explain why it is not required to be filed pursuant to Item 601(b)(10) of Regulation S-K.

Description of Capital Stock, page 139

18. We note that your current certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on your behalf. Please tell us whether the amended and restated certificate of incorporation that is to be in effect upon closing of the offering will contain a similar or a modified provision.

General

19. Please provide us proofs of all graphics, visual, or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note that we may have comments regarding this material.

20. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.

You may contact Sisi Cheng at 202-551-5004 or Jim Rosenberg at 202-551-3679 if you have questions regarding comments on the financial statements and related matters. Please contact Jeffrey Gabor at 202-551-2544 or Joe McCann at 202-551-6262 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Healthcare & Insurance

cc: Andrew D. Thorpe, Esq.