Orrick, Herrington & Sutcliffe LLP
1000 Marsh Road
Menlo Park, CA 94025-1015

+1 650 614 7400

orrick.com

April 29, 2019

Via EDGAR

Suzanne Hayes
Assistant Director, Office of Healthcare & Insurance
Division of Corporation Finance
United States Securities and Exchange Commission
100 F Street, N.E.
Washington, DC 20549

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

Dear Ms. Hayes:

On behalf of our client, Cortexyme, Inc. (the "Company"), we submit this letter to the Staff of the Securities and Exchange Commission (the "Commission") with respect to the above referenced Draft Registration Statement on Form S-1 (the "Draft Registration Statement"). Set forth below are the Company's responses to the comments contained in the Staff's letter dated April 25, 2019. The Staff's comments are repeated below in bold face type and followed by the Company's responses in regular type. Concurrent with this letter, the Company is filing its Registration Statement on Form S-1/A (the "Registration Statement"), which incorporates the Company's responses to the Staff's comments. The page references set forth in the Company's responses below are to the Registration Statement. For the Staff's reference, we have included both a clean copy of the Registration Statement and a copy marked to show all changes from the version filed on April 16, 2019.

Amendment No. 1 to Registration Statement on Form S-1 Filed April 16, 2019
Summary of Our Clinical and Preclinical Data, page 86

1. **We note your revisions in response to prior comment 4. Please revise the descriptions of the fifth and sixth studies to indicate the type of cells studied. Also tell us where in the prospectus you discuss the final study referenced in the table**.

Response:

In response to the Staff's comment, the Company has revised the table on pages 88 and 89 of the prospectus to reference human SH-SY5Y cells, which is a neuroblastoma cell line from human neural tissue commonly used in neuroscience research, that was used in the fifth study. In the same table, the Company clarified that the sixth study is a mouse brain study.

The final study is discussed in the prospectus on pages 95 and 100 of the prospectus. On page 95, the prospectus states, "However, among the identified gingipain substrates we have documented, tau is a target of gingipain proteolysis and potentially contributes to the development and toxicity of tau tangles." In addition, on page 100 of the prospectus, the Company discussed how ApoE, a target for gingipains, can be proteolytically cleaved into peptides consistent with those identified by other researchers in the brain and by the Company in the cerebral spinal fluid, or CSF, of Alzheimer's patients. In the Alzheimer's patients treated with COR388, fragments of ApoE in the CSF were reduced compared to placebo.

Exploratory Cognitive Testing, page 99

2. We note your response to prior comment 14 and note your revisions in this section and in the Summary. Please tell us whether the three WLA measurements you present are the only WLA parameters that you consider to be key measurements for indicating the presence and severity of Alzheimer's disease. In your response, tell us about the WLA testing that you will conduct in your Phase 2/3 GAIN trial, including whether all 35 markers will be assessed.

Response:

The Company's Phase 1b clinical trial was an exploratory study to look for the drug effects of COR388 with appropriate statistical methods, as noted on page 101 of the prospectus. Accordingly, the Company analyzed 35 speech parameters using Winterlight's technology. Because WLA is a relatively new platform, there is limited evidence indicating which of the 35 parameters are best for measuring the cognitive impairment in Alzheimer's patients, and the effects of Alzheimer's investigational treatments. It is a common technique in early clinical development to include a large number of readouts for the purpose of identifying those with a signal to include in future studies. Correcting for multiple analyses, using statistical methods such as the conservative Bonferonni correction, as discussed in the Registration Statement, is important in order to control for Type 1 error, or the increased chance of seeing significance on any single measure the more measures that are conducted. Standard statistics as well as Bonferonni corrected statistics are generally reported as the Company has done in the Registration Statement.

The three WLA measurements that the Company discusses in detail in the prospectus might not be the only measurements for indicating the presence and severity of Alzheimer's disease. The Company reports in detail on the three "key parameters" in its Phase 1b study because those parameters: (i) are clearly identified in the scientific literature as some of the most important parameters in Alzheimer's disease; (ii) impact communication and daily functions of Alzheimer's disease patients (please see improvement in a patient's communication in the example below); and (iii) were shown to be useful in measuring the effects of COR388. The 32 other parameters that were not discussed in detail in the prospectus either showed trends of improvement that were not statistically significant, or showed no meaningful changes over the course of the study. Additionally, the placebo group did not show any statistically significant improvements in any of the 35 measures.

In response to the Staff's comment, the Company has amended page 101 of the prospectus to include additional description of the results.

The statistical analysis plan for including WLA parameters in the GAIN study is still being finalized, but the Company intends to focus only on the key parameters identified as useful for measuring potential effects of COR388 on Alzheimer's disease. In response to the Staff's comment, the Company has amended page 101 of the prospectus to clarify that the Company will not include all 35 WLA parameters in the statistical analysis plan for the GAIN trial.

Example

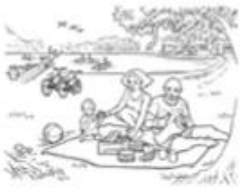
Winterlight: Examples of speech in 75-year-old female with moderate AD before and after COR388 treatment.

Transcript example Day 1

(...) = pause
(xxx) = unintelligible
Bold = preposition

"(...)(xxx) Uh (...) Table. Cat. Mouse. (...) Chair (...) Plant (...) Couch (...) Car (...) Curtain (...) Clock (...) Hanging Light..."

Transcript example Day 28



(...) = pause
(xxx) = unintelligible
Bold = preposition

"(...) Oh. well (xxx) Um. (...) A rowboat **with** two people (...) A garbage can (...) Two kayaks (...) A man's (...) about **to** fall off **of** a ramp (...) Two bicycles. Uh (...) two boats each **with** two people **in** them..."

We appreciate your time and attention to the Company's responses to the Staff's comments. Should you have any additional questions or concerns, please call me at (415) 773-5970.

Very truly yours,

/s/ Andrew D. Thorpe
Andrew D. Thorpe

cc: Casey C. Lynch, Cortexyme, Inc.
Christopher Lowe, Cortexyme, Inc.
Kristin Gafric, Esq., Cortexyme, Inc.
Scott Iyama, Esq., Orrick, Herrington & Sutcliffe LLP
Peter Lamb, Esq., Orrick, Herrington & Sutcliffe LLP
Brian J. Cuneo, Esq., Latham & Watkins LLP
B. Shayne Kennedy, Esq., Latham & Watkins LLP
Ross McAloon, Esq., Latham & Watkins LLP
Jeffrey Gabor, Esq., Securities & Exchange Commission
Joseph McCann, Esq., Securities & Exchange Commission