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May 5, 2022

U.S. Securities and Exchange Commission
Division of Corporation Finance
100 F Street, N.E.
Washington, DC 20549

Attn: Tim Buchmiller
Jason Drory
Eric Atallah
Lynn Dicker

Re: Lexeo Therapeutics, Inc.
Draft Registration Statement on Form S-1
Submitted February 4, 2022
CIK No. 0001907108

Ladies and Gentlemen:

On behalf of Lexeo Therapeutics, Inc. (the "***Company***"), we are providing this letter in response to the comments of the staff (the "***Staff***") of the U.S. Securities and Exchange Commission (the "***Commission***") Division of Corporation Finance contained in its letter, dated March 3, 2022 (the "***Comment Letter***"), relating to the Company's Draft Registration Statement on Form S-1, confidentially submitted on February 4, 2022 (the "***Draft Registration Statement***").

The Company is concurrently confidentially submitting Amendment No. 1 to the Draft Registration Statement on Form S-1 (the "***Amendment No. 1***"), which reflects changes made in response to certain of the comments contained in the Comment Letter.

The numbering of the paragraphs below corresponds to the numbering of the comments contained in the Comment Letter, which for your convenience we have incorporated into this response letter in italics. Page references in the text of this response letter correspond to the page numbers of Amendment No. 1. Capitalized terms used but not otherwise defined in this letter shall have the meanings set forth in Amendment No. 1.

Draft Registration Statement on Form S-1 submitted February 4, 2022

Prospectus summary

Overview, page 1

1. *We note your disclosure here and throughout that you are focused on "diseases affecting both larger-rare and prevalent patient populations." However, we note your disclosure at the bottom of page 4 that depicts CLN2 Batten disease as an "Ultra Rare Disease," which appears to be your indication for your LX1004 product candidate. Please update your disclosure here to clarify that your most advanced product candidate is an "Ultra Rare Disease" or otherwise advise.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised pages 5 and 131 of Amendment No. 1.

Lead cardiovascular programs, page 2

2. *We note your disclosure at the top of page 3 that, "in [y]our preclinical studies, LX2020 resulted in fewer arrhythmias and increased survival." Please revise your disclosure here to clearly state, if true, that the studies performed to date were animal trials. In this regard, we note your disclosure on page 138.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised pages 3 and 123 of Amendment No. 1.

Our pipeline, page 2

3. *We note the inclusion of product candidates in your pipeline table, which appear to still be in the "discovery" phase. In addition, we note your disclosure elsewhere on page 33 where you state you "are primarily focused on the development of LX2006, LX1001 and LX1004" and your intellectual property disclosure on page 151 only appears to describe patents and pending patents related to LX2006, LX1020 and LX1021. Given the limited amount of disclosure related to your programs in discovery, please explain why these programs are sufficiently material to your business to warrant inclusion in your pipeline table. If they are material, please expand your disclosure in your Business section to provide a more fulsome discussion of these programs, including a description of preclinical studies or development activities conducted and expand your intellectual property disclosure if applicable. Alternatively, remove any programs that are not currently material from your pipeline table on pages 2 and 120.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised pages 2, 3, 4, 34, 124, 125, 129, 135, 136, 144, 145, 146, 151, 152, 153 and 160 of Amendment No. 1 to provide a more fulsome discussion of its discovery-stage programs.

4. *Please revise your pipeline table to include separate columns for Phase 1, Phase 2 and Phase 3 trials or tell us the basis for your belief that you will be able to conduct Phase 1/2 and Phase 2/3 trials for all your product candidates.*

Response: The Company respectfully advises the Staff that it believes that the pipeline table on pages 2 and 123 of Amendment No. 1 appropriately reflects its planned clinical development programs.

The typical drug development process includes Phase 1 first-in-human clinical trials, which are typically conducted in healthy adult volunteers, followed by Phase 2 clinical trials in patients with the disease to demonstrate safety and preliminary efficacy in the targeted patient population. FDA's June 2015 final guidance entitled *Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products* ("FDA's June 2015 final guidance") states that it is generally not accepted that gene therapy product candidates be administered to healthy volunteers. These treatments have the potential for serious and unintended effects that may be permanent, along with adverse effects due to invasive procedures that may be necessary for product administration, which lead to an unacceptable risk-benefit profile for healthy volunteers. Additionally, in FDA's June 2015 final guidance, the FDA notes that sponsors of gene therapy products "should consider the design of early-phase studies in the context of the objectives of the overall development program…For example, some Phase 1 studies include selected features of Phase 2 study design in order to gather preliminary evidence of effectiveness." Accordingly, the Company intends to evaluate its product candidates in a limited patient population in combined Phase 1/2 trials, which the Company notes is consistent with the clinical development approach taken by sponsors of other gene therapy products that have received FDA approval following a Phase 1/2 clinical trial. As described in Amendment No. 1, each of the Company's planned Phase 1/2 trials will involve an evaluation of safety of the product candidate as they will involve the initial introduction of a new product candidate in humans, as well as preliminary evaluations of efficacy of the product candidate because they are being administered to patients with the disease being targeted for treatment.

Furthermore, the FDA's January 2020 final guidance entitled *Human Gene Therapy for Rare Diseases* states that sponsors of gene therapy clinical trials "should consider designing their first-in-human study to be an adequate and well-controlled investigation that has the potential, depending on the study results, to provide evidence of effectiveness to support a marketing application." In accordance with this guidance, a pivotal clinical trial intended to support a BLA may not necessarily be denoted as a Phase 3 clinical trial. The Company further notes that some currently approved gene therapy products and rare disease products have received FDA approval following a Phase 1/2 clinical trial, without being tested in a Phase 3 trial, or have received approval following a pivotal clinical trial that was not specifically designated as Phase 3. The Company plans to design all of its Phase 2/3 clinical trials so that each has the potential, depending on the trial results, to support a marketing application. Thus, the combination of Phase 2 and Phase 3 into a single column is representative of the Company's intended clinical development for each of its programs.

5. *We note your pipeline table states that LX1004's upcoming milestone is "1H 2023: Pivotal Study Start." However, your disclosure on page 3 indicates that you, "anticipate receiving feedback from the FDA on the design of [y]our potentially pivotal Phase 2/3 clinical trial in the second half of 2022." Please revise your disclosure in the pipeline table and elsewhere, as applicable, to make it clear, if true, that the U.S. Food and Drug Administration (FDA) or other regulators may require you to conduct sequential trials.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised pages 2, 4, 123, 125 and 157 of Amendment No. 1.

High Transduction Efficiency and Biodistribution, page 4

6. *We note your disclosure here and elsewhere that the AAVrh10 vector is "optimal for delivery and expression of transgenes for the treatment of the cardiovascular and CNS diseases [you] are currently targeting." However, we note your disclosure on page 129 that you are collaborating with Weill Cornell Medicine on the discovery of second and third generation cardiac vector technology. Please provide your basis for your belief that the AAVrh10 vector is "optimal" or otherwise advise.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised pages 4 and 129 of Amendment No. 1.

7. *If your disclosure that the AAVrh10 vector has proven to be "effective at transducing myocardial cells and neurons" is based on preclinical studies on non-human cells, please make that clear. In this regard, we note from your disclosure on page 126 that this disclosure appears to be based on your preclinical studies on nonhuman primates and murine models.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised pages 4 and 129 of Amendment No. 1.

Our disease area strategy, page 4

8. *We note your reference in the graphic at the bottom of page 4 to "early evidence of clinical benefit" as well as "promising preclinical data." In addition, we note your disclosure on page 144 that "LX1001 has promise as a therapeutic for APOE4 homozygous Alzheimer's disease patients." As safety and efficacy determinations are solely within the FDA's authority and they continue to be evaluated throughout all phases of clinical trials, please remove these and any such references in your prospectus. In the Business section, you may present objective data resulting from your trials without including conclusions related to efficacy.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised pages 1, 5, 6, 122, 131, 132 and 151 of Amendment No. 1.

Our company and team, page 6

9. *We note that you identify certain "premier institutional investors" in your company in this section. Please limit the disclosure of specific investors to those identified in the principal stockholders table on page 198. Additionally, indicate that prospective investors should not rely on the named investors' investment decision, that these investors may have different risk tolerances and the recent offering was conducted as a significant discount to the IPO price.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised pages 7 and 126 of Amendment No. 1 to remove the reference to premier institutional investors and to clarify that the investors are funds affiliated with the named entities.

Risks associated with our business, page 7

10. *Please revise your risk factor summary to highlight that you currently do not own or license any composition of matter patents or patent applications covering your LX1001 and LX1004 product candidates, consistent with your disclosure on page 56. Please add similar clarifying disclosure in the "Intellectual property" section beginning on page 151.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised pages 8 and 159 of Amendment No. 1.

Research collaboration agreement with Weill Cornell Medicine, page 104

11. *We note your disclosure on page 46 that "[y]our collaboration with Cornell University is critical to [y]our business." Please file the Research Collaboration Agreement with Weill Cornell Medicine as an exhibit to the registration statement as required by Item 601(b)(10) of Regulation S-K or tell us why it is not material.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised page 107 of Amendment No. 1. The Company will file in a future amendment the Research Collaboration Agreement with Weill Cornell Medicine as required by Item 601(b)(10) of Regulation S-K.

Exclusive license agreement with the Regents of the University of California, San Diego, page 105

12. *We note your disclosure in this section regarding the UCSD Agreement and your disclosure on page 124 that your foundational science stems in part from your license agreement with UCSD. Please file the agreement as an exhibit to the registration statement, or provide your analysis supporting your conclusion that filing is not required. See Item 601(b)(10) of Regulation S-K for guidance. In addition, please update your disclosure to clarify which product candidate(s) are covered by the license agreement or otherwise advise.*

   Response: The Company respectfully acknowledges the Staff's comment and has revised page 107 of Amendment No. 1. The Company will file in a future amendment the license agreement with UCSD as required by Item 601(b)(10) of Regulation S-K.

Stelios Therapeutics Inc. acquisition, page 105

13. *Please file the Stelios Therapeutics Inc. acquisition agreement as an exhibit to the registration statement or tell us why you are not required to do so. Refer to Item 601(b)(2) of Regulation S-K. In addition, please disclose more specific information about the "certain milestones" that must be reached in order for you to pay the additional $20.5 million in payments, including identifying the specific product candidate(s) that relate to the agreement or otherwise advise.*

Response: The Company respectfully acknowledges the Staff's comment and has revised page 107 of Amendment No. 1. Additionally, the Company will file in a future amendment the Stelios Therapeutics Inc. acquisition agreement as required by Item 601(b)(2) of Regulation S-K.

Management's Discussion and Analysis of Financial Condition and Results of Operations

Critical Accounting Policies and Significant Judgements and Estimates

Determination of Fair Value of Common Stock, page 115

14. *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. Please discuss with the staff how to submit your response.*

Response: The Company respectfully advises the Staff that it will provide the Staff with the requested information once an estimated offering price range has been determined by the Company and the underwriters and will contact the Staff to discuss its delivery.

Our strategy, page 123

15. *We note your statement here that you established "a leading cardiovascular gene therapy pipeline." Please revise to disclose the basis for this statement.*

Response: The Company respectfully acknowledges the Staff's comment and has revised pages 127 and 133 of Amendment No. 1.

Preclinical safety studies, page 135

16. *We note your disclosure here that, "large body of available data suggests that HCC observed in mice after AAV treatment is unlikely to translate to risks for humans, as it has not been observed in higher species or humans (FDA 2021)." Please elaborate on and clarify what you mean by "large body of available data" and "(FDA 2021)," which appears at the end of the sentence.*

Response: The Company respectfully acknowledges the Staff's comment and has revised pages 27 and 140 of Amendment No. 1.

Phase 1/2 clinical trial results, page 147

17. *We note your disclosure at the top of page 149 discloses that there were "minimal serious adverse events." Please update your disclosure to disclose what the serious adverse events were and how many subjects experienced them.*

Response: The Company respectfully acknowledges the Staff's comment and has revised pages 27 and 157 of Amendment No. 1.

Manufacturing, page 151

18. *We note your disclosure here that you have partnered with Virovek, Inc., Millipore Corporation and Fujifilm Diosynth Biotechnologies U.S.A., Inc. in connection with manufacturing your vector product candidates. Please update your disclosure here to disclose the material terms of your manufacturing agreements and please file these agreements as exhibits to the registration statement as required by Item 601(b)(10) of Regulation S-K or tell us why they are not material.*

Response: The Company acknowledges the Staff's comment but respectfully advises the Staff that it does not believe its manufacturing agreements with Virovek, Inc., Millipore Corporation and Fujifilm Diosynth Biotechnologies U.S.A., Inc. are required to be described or to be filed as material agreements under Item 601(b)(10) of Regulation S-K.

Item 601(b)(10)(i) of Regulation S-K defines a "material contract" as a contract made outside of the ordinary course of business which is material to the registrant. Item 601(b)(10)(ii)(B) of Regulation S-K clarifies that if an agreement is such as ordinarily accompanies the kind of business conducted by the registrant, it will be deemed to be made in the ordinary course of business, and therefore not required to be filed, unless the agreement is, among other things, one "upon which the registrant's business is substantially dependent." The Company respectfully advises the Staff that each of the manufacturing agreements was entered into in the ordinary course of the Company's business, and that the Company is not substantially dependent upon any of these agreements.

As described in Amendment No. 1, the Company is a clinical-stage gene therapy company focused on treatments for diseases affecting both larger-rare and prevalent patient populations. The Company has disclosed in Amendment No. 1 that developing gene therapy candidates for larger-rare and prevalent disease patient populations requires a high-quality process that can produce vector in relatively large quantities while utilizing established biologics manufacturing infrastructure. As a result, the Company would be expected to enter into manufacturing agreements from time to time in order to produce such vectors as well as the related gene therapy candidates. Such manufacturing agreements would ordinarily accompany the business of producing vectors and gene therapy candidates.

The Company respectfully submits that these manufacturing agreements do not fall within subsections A, C or D of Item 601(b)(10)(ii). Furthermore, because there are other manufacturers available that would be able to meet the Company's requirements if it needed to change manufacturers and because the Company is currently

evaluating other manufacturing partners, the Company respectfully advises the Staff that subsection B of Item 601(b)(10)(ii) of Regulation S-K is inapplicable because the Company's business is not "substantially dependent" on any of its manufacturing agreements with Virovek, Inc., Millipore Corporation or Fujifilm Diosynth Biotechnologies U.S.A., Inc.

For the foregoing reasons, the Company respectfully advises the Staff that it does not consider any of the manufacturing agreements to satisfy the definition of a "material contract" under Item 601(b)(10)(i) of Regulation S-K. Furthermore, the Company respectfully advises the Staff that it does not believe filing any of the agreements as an exhibit would provide meaningful information to investors beyond that which has already been summarized in Amendment No. 1. The Company advises the Staff that it will continue to evaluate in future periods whether any of the manufacturing agreements satisfy the definition of a "material contract" under Item 601(b)(10) of Regulation S-K.

License agreements, page 152

19. *Please revise your disclosure to include the aggregate milestone payments due under each of the license agreements with Cornell University.*

Response: The Company respectfully acknowledges the Staff's comment and has revised pages 161 and 162 of Amendment No. 1.

Agreements with our named executive officers, page 180

20. *Please file the employment agreements you have entered into with your named executive officers. Refer to Item 601(b)(10) of Regulation S-K.*

Response: The Company respectfully acknowledges the Staff's comment and will file in a future amendment all employment agreements required by Item 601(b)(10) of Regulation S-K.

2022 equity incentive plan, page 183

21. *We note your disclosure on page 184 that the administrator of the 2022 Plan has the power to modify awards under your 2022 Plan, including the authority to reprice any outstanding option or stock appreciation right, or take any other action that is treated as a repricing. Please clarify if these repricing actions would require stockholder approval. If such actions would not require stockholder approval, please include appropriate risk factor disclosure, including whether proxy advisory firms could find such repricing without stockholder approval contrary to a performance-based pay philosophy.*

Response: The Company respectfully acknowledges the Staff's comment and has revised page 192 of Amendment No. 1.

Certain relationships and related party transactions

Agreements with Ronald G. Crystal, M.D., page 194

22. *Please file the agreements disclosed in this section as exhibits as required by Item 601(b)(10) of Regulation S-K, or tell us why you believe they are not required to be filed.*

Response: The Company respectfully acknowledges the Staff's comment and will file in a future amendment the agreements disclosed in this section as required by Item 601(b)(10) of Regulation S-K.

General

23. *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.*

Response: The Company respectfully acknowledges the Staff's comment and will provide the Staff with copies of all written communications, as defined in Rule 405 under the Securities Act, that the Company, or anyone authorized to do so on its behalf, presents to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.

* * * *

Please direct any questions or further comments concerning Amendment No. 1 or this response letter to either the undersigned at (212) 479-6565 or Dayne Brown of Cooley LLP at (212) 479-6712.

Sincerely,

/s/ Eric Blanchard

Eric Blanchard

cc: R. Nolan Townsend, Lexeo Therapeutics, Inc.
Jenny Robertson, Lexeo Therapeutics, Inc.
Dayne Brown, Cooley LLP
Peter Byrne, Cooley LLP
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