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

DIVISION OF
CORPORATION FINANCE

June 20, 2021

René Russo, Pharm.D.
President and Chief Executive Officer
Xilio Therapeutics, Inc.
828 Winter Street
Waltham, Massachusetts 02451

Re: Xilio Therapeutics, Inc.
Draft Registration Statement on Form S-1
Submitted May 24, 2021
CIK No. 0001840233

Dear Dr. Russo:

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

Our Pipeline, page 4

1. Please include the indication for each program in the pipeline table here and on page 117.

Overview, page 4

2. We note your disclosure that cytokines have demonstrated the ability to generate sustained complete responses. If this disclosure is based on the data in the chart presented on page 112, please balance your disclosure to indicate, if true, that only a small subset of patients who received high-dose IL-2 achieved a complete response, or tell us the basis for this disclosure. Please also disclose the nature of the “compelling clinical efficacy” demonstrated by cytokines in certain tumors.

Our GPS Platform, page 6

3. We note your disclosure that your engineered molecules are designed to be turned on selectively in the TME, thereby reducing potential toxicities and improving their therapeutic index. We note, however, that some of your statements in this section and elsewhere indicate less activity outside of the TME and some statements indicate no activity. For example, we note your disclosure in this section that MMPs are "preferentially active" in the TME by comparison to non-tumor organs or tissues, and that your GPS-enabled cytokines minimize or reduce the risk of activity outside of the TME and, therefore, the risk of toxicity. Given those disclosures, please tell us why your disclosure in this section that MMP activity can be leveraged to activate molecules within the TME that "remain inactive outside of the TME", and that the features of your GPS-enabled molecules work in concert to enable your molecules' potential ability to induce tumor selective biological activity and tumor growth inhibition "without toxicity outside of the TME," are appropriate, or revise your disclosure as necessary.

Our History and Team, page 7

4. We note that you identify certain entities as investors in your company here and on page 107. However, certain of these entities do not appear to be among your principal stockholders as disclosed on page 186. If material, please expand your disclosure to describe the nature of each such entity's investment in you and explain to us why including this information is appropriate. Please also explain in the response your plans to update investors about any changes these entities make with respect to their investments in your company.

Our Strategy, page 8

5. We note your disclosure here and throughout the prospectus comparing XTX202 to aldesleukin, and XTX101 to an ipilimumab analog. Please clarify, if true, that these observations were made in mouse models and may not be replicated in clinical trials.

Risk Factors, page 16

6. Given the length of your risk factor section, please revise to comply with Regulation S-K Item 105 by relocating risks that could generically apply to any registrant or offering to the end of the section under the caption "General Risk Factors."

Some intellectual property that we have in-licensed may have been discovered through government funded programs, page 52

7. Please revise to identify the product candidates that are or may be subject to march-in rights.

Capitalization, page 82

8. Please revise to reflect the convertible preferred stock outside of permanent equity consistent with your interim balance sheet on page F-40.

Dilution, page 84

9. Please revise your disclosure to clarify that historical net tangible book value (deficit) excludes convertible preferred stock classified outside of equity.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies and Use of Estimates
Determination of Fair Value of Common Units and Common Stock, page 104

10. Please disclose the actual specific factors underlying the increase in the May 2021 common stock valuation to $1.06.

Business
Key Features of Our GPS-Enabled Cytokines, page 114

11. We note your disclosure on pages 115 and 116 that you have validated your GPS platform through your preclinical studies with XTX202 and by your tumor-selective anti-CTLA-4 antibody. Please revise to explain what you mean by validated given the current stage of development of your product candidates.

Cytokine programs, page 117

12. We note your disclosure on page 27 that you rely on matrix metalloproteases to activate your molecules within the tumor microenvironment and that if MMP activity in human tumors is not sufficient to cleave the masking protein domain, the potential efficacy of your product candidates would be limited. For each of your cytokine programs, please clarify whether you have observed that the MMPs native to human cells are sufficient to cleave the masking domain.

Measured PK Parameters (1 mg/kg dose), page 123

13. We note your statement that you expect XTX202 to achieve monotherapy activity in clinical trials and have a better tolerability profile than aldesleukin based on your preclinical data. Given the unpredictability of drug development, please remove this statement and any similar statements as such statements would appear to be speculative.

Principal Stockholders, page 186

14. Please revise your disclosure to identify all of the natural person or persons who have voting and investment control of the shares held by the entities affiliated with Atlas Ventures, F-Prime Capital Partners Healthcare Fund IV LP and affiliates, Takeda Ventures, Inc. and SV7 Impact Medicine Fund LP.

General

15. 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 Michael Fay at (202) 551-3812 or Vanessa Robertson at (202) 551-3649 if you have questions regarding comments on the financial statements and related matters. Please contact Ada Sarmento at (202) 551-3798 or Tim Buchmiller at (202) 551-3635 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Life Sciences

cc: Cynthia T. Mazareas, Esq.