



DIVISION OF
CORPORATION FINANCE

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

August 20, 2024

E. Rand Sutherland
Chief Executive Officer
Upstream Bio, Inc.
460 Totten Pond Road, Suite 420
Waltham, MA 02451

**Re: Upstream Bio, Inc.
Amendment No. 2 to Draft Registration Statement on Form S-1
Submitted August 9, 2024
CIK No. 0002022626**

Dear E. Rand Sutherland:

We have reviewed your amended draft registration statement and have the following comment.

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 this comment applies 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 this letter and your amended draft registration statement or filed registration statement, we may have additional comments. Unless we note otherwise, any references to prior comments are to comments in our July 25, 2024 letter.

Amendment No. 2 to Draft Registration Statement on Form S-1

Prospectus Summary

Overview, page 1

1. We note your response to comment 5. Please disclose and quantify any SAEs with respect to the referenced trials for tezepelumab. In addition, please briefly describe interleukin ("IL")-4 receptor alpha antagonist and how this differs from your approach targeting the TSLP pathway.

Please contact Franklin Wyman at 202-551-3660 or Kevin Kuhar at 202-551-3662 if you have questions regarding comments on the financial statements and related matters. Please contact Jimmy McNamara at 202-551-7349 or Chris Edwards at 202-551-6761 with any other

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questions.

Sincerely,

Division of Corporation Finance
Office of Life Sciences

cc: Gabriela Morales-Rivera