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

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of report (date of earliest event reported): May 06, 2025

UPSTREAM BIO, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-42366**	**38-4187694**
(State or other jurisdiction of incorporation)	**(Commission file number)**	**(IRS employer identification no.)**
890 Winter Street Suite 200 Waltham, Massachusetts		**02451**
(Address of principal executive offices)		**(Zip code)**

Registrant's telephone number, including area code: (781) 208-2466

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	UPB	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

On May 6, 2025, Upstream Bio, Inc. (the "Company") announced its financial results and business highlights for the quarter ended March 31, 2025. A copy of the press release is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information included under Item 2.02 of this Current Report on Form 8-K, including Exhibit 99.1, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, and shall not be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1	Press Release issued by Upstream Bio, Inc. on May 6, 2025, furnished herewith.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Upstream Bio, Inc.

Date: May 6, 2025

By: /s/ E. Rand Sutherland
E. Rand Sutherland, M.D.
Chief Executive Officer

Upstream Bio Reports First Quarter 2025 Financial Results and Accelerates Guidance on All Clinical Programs

– Top-line data from Phase 2 clinical trial of verekitug in patients with chronic rhinosinusitis with nasal polyps expected in the third quarter of 2025 –

– Top-line data from Phase 2 clinical trial of verekitug in patients with severe asthma now expected in the first half of 2026 –

– First patient in Phase 2 clinical trial of verekitug in patients with chronic obstructive pulmonary disease to be dosed in mid-2025 –

WALTHAM, Mass. – May 6, 2025 - Upstream Bio, Inc. (Nasdaq: UPB), a clinical-stage company developing treatments for inflammatory diseases, with an initial focus on severe respiratory disorders, today reported financial results for the first quarter ended March 31, 2025, and provided a summary of recent business highlights. The Company is developing verekitug, the only monoclonal antibody currently in clinical development that targets and inhibits the thymic stromal lymphopoietin (TSLP) receptor, in multiple severe respiratory diseases including chronic rhinosinusitis with nasal polyps (CRSwNP), severe asthma and chronic obstructive pulmonary disease (COPD).

“This quarter we made excellent progress in our development of verekitug, positioning us well to deliver on our upcoming clinical milestones. We are pleased to accelerate our guidance on several near-term events, including the top-line data readout from our Phase 2 clinical trial of verekitug in patients with CRSwNP, expected in the third quarter of this year,” said Rand Sutherland, MD, Chief Executive Officer of Upstream Bio. “In addition, we now anticipate reporting top-line data from our Phase 2 clinical trial in severe asthma in the first half of 2026. We also now expect to dose the first patient in our Phase 2 clinical trial in COPD in mid-2025. We look forward to sharing further updates as we reach these key milestones.”

Dr. Sutherland continued, “Verekitug is the only known molecule currently in clinical development targeting the TSLP receptor. Early clinical data suggest that this unique mechanism of action has the potential to meaningfully impact disease activity in patients with these severe respiratory diseases through both differentiated efficacy and an extended dosing interval, and we are testing the therapeutic implications of these observations across our development programs.”

First Quarter 2025 and Recent Business Highlights

- **Top-line data from Phase 2 clinical trial in patients with CRSwNP expected in the third quarter of 2025:** In January 2025, Upstream Bio completed patient enrollment in its Phase 2 multicenter, randomized, placebo-controlled, parallel group clinical trial designed to assess the efficacy and safety of verekitug in participants with CRSwNP. Top-line data from this clinical trial is expected to be reported in the third quarter of 2025.

  The Company has designed this trial using endpoints that, pending interactions with regulatory authorities, could produce data to support submissions for product approval. Patients were

randomized to receive either 100 mg of verekitug or placebo administered subcutaneously every 12 weeks over a 24-week treatment period. The primary endpoint is change from baseline in nasal polyp score (NPS) at week 24, a primary endpoint that has been used in several registrational trials for other biologic treatments for CRSwNP. Secondary endpoints include: nasal congestion score, sinus opacification, difficulty with sense of smell, nasal symptoms, percentage of participants requiring systemic corticosteroids or nasal polyp surgery, time to nasal polyp surgery and/or time to systemic corticosteroids for nasal polyps, total symptom score, and characterization of safety.

- **Top-line data from Phase 2 clinical trial in patients with severe asthma now expected in the first half of 2026:** The Company has designed this trial using endpoints that, pending interactions with regulatory authorities, could produce data to support submissions for product approval.

  Upstream Bio also plans to initiate a long-term safety and efficacy extension study (Phase 2 LTE) in certain adult patients with severe asthma following completion of its Phase 2 severe asthma trial with the first patient expected to transition to the LTE study in the second quarter of 2025.

- **First patient dosing in Phase 2 clinical trial in COPD expected in mid-2025:** Upstream Bio is initiating development of verekitug in a Phase 2 clinical trial in patients with moderate-to-severe COPD and now expects to dose the first patient in mid-2025.

  The Company has designed this trial using endpoints that, pending interactions with regulatory authorities, could produce data to support submissions for product approval.

First Quarter 2025 Financial Results

As of March 31, 2025, Upstream Bio had cash, cash equivalents and short-term investments of $431.4 million, which is expected to fund planned operations through 2027.

Research and development expenses were $25.8 million for the quarter ended March 31, 2025, compared to $11.7 million for the same period in 2024. The increase of $14.1 million was primarily driven by an increase in clinical and manufacturing expenses related to the Company's verekitug program.

General and administrative expenses were $6.8 million for the quarter ended March 31, 2025, compared to $4.0 million for the same period in 2024. The increase of $2.8 million was primarily driven by an increase in personnel-related expenses, including share-based compensation, and professional service fees.

Net loss was $27.3 million for the quarter ended March 31, 2025, compared to a net loss of $10.9 million for the same period in 2024. The increase of $16.4 million was largely due to increased research and development and general and administrative expenses, partially offset by increased interest income.

Upcoming Events

Upstream Bio expects to participate in the following investor conferences and medical congresses:

- Goldman Sachs 46th Annual Global Healthcare Conference 2025, Miami, FL, Upstream Bio presentation on June 11, 2025, at 9:20 a.m. ET

- European Academy of Allergy and Clinical Immunology (EAACI) Congress 2025, Glasgow, United Kingdom, June 13-16, 2025

About Upstream Bio

Upstream Bio is a clinical-stage biotechnology company developing treatments for inflammatory diseases, with an initial focus on severe respiratory disorders. Upstream Bio is developing verekitug, the only known antagonist currently in clinical development that targets the receptor for thymic stromal lymphopoietin, a cytokine which is a clinically validated driver of inflammatory response positioned upstream of multiple signaling cascades that affect a variety of immune mediated diseases. Upstream Bio has advanced this highly potent monoclonal antibody into separate Phase 2 trials for the treatment of severe asthma and chronic rhinosinusitis with nasal polyps and is initiating development in chronic obstructive pulmonary disease. Upstream Bio's team is committed to maximizing verekitug's unique attributes to address the substantial unmet needs for patients underserved by today's standard of care. To learn more, please visit www.upstreambio.com.

Upstream Bio intends to use the investor relations page on its website as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD. Accordingly, investors should monitor its website in addition to following press releases, filings with the Securities and Exchange Commission (SEC), public conference calls, presentations and webcasts.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. These statements may be identified by words such as "aims," "anticipates," "believes," "continue," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "predict," "project," "seeks," "should," "target," "will" and variations of these words or similar expressions. Any statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements. These forward-looking statements include, without limitation, express or implied statements regarding: the clinical development of verekitug for the treatment of severe asthma, CRSwNP and COPD, including the initiation, timing, progress and results of ongoing and planned clinical trials; expectations for future discussions with regulatory authorities and the potential of the endpoints of the Company's clinical trials to produce data that could support submissions for product approval; expectations regarding the safety, efficacy or tolerability of verekitug; Upstream Bio's expected operating expenses and capital expenditure requirements, including its cash runway through 2027; and participation at upcoming investor conferences and medical congresses. Any forward-looking statements in this press release are based on the Company's current expectations, estimates and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Readers are cautioned that actual results, levels of activity, safety, efficacy, performance or events and circumstances could differ materially from those expressed or implied in the Company's forward-looking statements due to a variety of risks and uncertainties, which include, without limitation, risks and uncertainties related to: Upstream Bio's ability to advance verekitug through clinical development, and to obtain regulatory approval of and ultimately commercialize verekitug on the expected timeline, if at all; the initiation, timing, progress and results of clinical trials; Upstream Bio's ability to fund its development activities and achieve development goals; Upstream Bio's dependence on third parties to conduct clinical trials and manufacture

verekitug, and commercialize verekitug, if approved; Upstream Bio's ability to attract, hire and retain key personnel, and protect its intellectual property; Upstream Bio's financial condition and need for substantial additional funds in order to complete development activities and commercialize verekitug, if approved; regulatory developments and approval processes of the U.S. Food and Drug Administration and comparable foreign regulatory authorities; Upstream Bio's competitors and industry; and other risks and uncertainties described in greater detail under the caption "Risk Factors" in Upstream Bio's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as well as any subsequent filings with the SEC. Any forward-looking statements represent Upstream Bio's views only as of today and should not be relied upon as representing its views as of any subsequent date. Upstream Bio explicitly disclaims any obligation or undertaking to update any forward-looking statements contained herein to reflect any change in its expectations or any changes in events, conditions or circumstances on which any such statement is based except to the extent required by law, and claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Investor and Media Contact:
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UPSTREAM BIO, INC.
CONDENSED CONSOLIDATED BALANCE SHEET
(IN THOUSANDS)
(UNAUDITED)

	March 31, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 71,312	$ 325,892
Short-term investments	360,068	144,559
Accounts receivable	566	613
Prepaid expenses and other current assets	21,841	8,096
Total current assets	453,787	479,160
Property and equipment, net	539	582
Operating lease right-of-use assets	1,649	1,783
Restricted cash	194	194
Total assets	$ 456,169	$ 481,719
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 4,718	$ 4,041
Accrued expenses and other current liabilities	4,141	5,992
Operating lease liabilities, current portion	708	704
Total current liabilities	9,567	10,737
Operating lease liabilities, net of current portion	992	1,130
Total liabilities	10,559	11,867
Stockholders' equity:		
Common stock	53	53
Additional paid-in capital	663,239	660,604
Accumulated other comprehensive income (loss)	368	(25)
Accumulated deficit	(218,050)	(190,780)
Total stockholders' equity	445,610	469,852
Total liabilities and stockholders' equity	$ 456,169	$ 481,719

UPSTREAM BIO, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(IN THOUSANDS)
(UNAUDITED)

	Three Months Ended March 31,	
	2025	**2024**
Collaboration revenue	$ 566	$ 640
Operating expenses:		
Research and development	25,797	11,691
General and administrative	6,782	3,962
Total operating expenses	32,579	15,653
Loss from operations	(32,013)	(15,013)
Other income (expense):		
Change in fair value of preferred stock tranche right liability	—	2,859
Interest income	4,743	1,266
Other expense, net	—	(6)
Total other income, net	4,743	4,119
Net loss	$ (27,270)	$ (10,894)