



Upstream Bio Reports Third Quarter 2025 Financial Results and Highlights Continued Progress

November 5, 2025

– Positive top-line results from VIBRANT Phase 2 trial of verekitug in CRSwNP reported in September showed statistically significant and clinically meaningful effects on primary and key secondary endpoints when administered once every 12 weeks –

– On-track to report top-line results from VALIANT Phase 2 trial in severe asthma in the first quarter of 2026 –

– Enrollment ongoing in VENTURE Phase 2 trial in COPD; first patient dosed in July –

WALTHAM, Mass., Nov. 05, 2025 (GLOBE NEWSWIRE) -- [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 third quarter ended September 30, 2025, and provided a summary of recent business highlights. The Company is developing verekitug, the only known antagonist 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). Verekitug's unique pharmacology may lead to differentiated efficacy and an extended dosing interval as compared to the current standard of care.

"During this quarter we reached an important milestone in verekitug's development and shared positive top-line results from VIBRANT, our Phase 2 trial in CRSwNP, which reinforced verekitug's differentiated clinical profile, including its potential for efficacy meeting or exceeding that of available biologics, with administration only four times per year," said Rand Sutherland, MD, Chief Executive Officer of Upstream Bio. "We also continued to bolster our understanding of verekitug through translational research, including with the presentation of new data identifying structural and mechanistic drivers of verekitug's potent disruption of TSLP signaling by antagonism of the TSLP receptor at the European Respiratory Society Congress in September."

"We remain on track to report top-line results from VALIANT, our Phase 2 trial in severe asthma, in the first quarter of 2026. Guided by these data, and following discussion with regulators, we will be well-positioned to advance our Phase 3 development plans for verekitug in both CRSwNP and severe asthma," added Dr. Sutherland. "In addition, we continue to make investments in CMC and drug delivery with the goal of further strengthening the clinical profile and utility of verekitug for patients."

Recent Business Highlights and Upcoming Milestones

- **Positive top-line results from the VIBRANT Phase 2 trial in CRSwNP reported in September 2025:**

- Positive top-line results from the VIBRANT Phase 2 trial in CRSwNP showed statistically significant and clinically meaningful effects on multiple endpoints when administered once every 12 weeks.
 - In this 24-week study, VIBRANT met its primary endpoint, with verekitug dosed every 12 weeks leading to a statistically significant and clinically meaningful reduction from baseline in placebo-adjusted endoscopic nasal polyp score (NPS) of -1.8 ($p < 0.0001$). The observed clinical effect on endoscopic NPS in this Phase 2 trial suggests verekitug meets or exceeds that of other biologics in CRSwNP at 24 weeks.
 - Significant and clinically meaningful improvements were observed in key secondary endpoints, including -0.8 ($p = 0.0003$) reduction in nasal congestion score and 76% ($p = 0.03$) reduction in need for surgery or systemic corticosteroids.
 - Verekitug was generally well tolerated, demonstrating a favorable safety profile consistent with previous studies, with no serious adverse events (SAEs) observed.
 - The Company has designed this trial using endpoints that, pending interactions with regulatory authorities, could produce data to support submissions for product approval.

- **Top-line data from the VALIANT Phase 2 trial in severe asthma expected in the first quarter of 2026:**

- VALIANT is a Phase 2 global, randomized, double-blind, placebo-controlled, parallel group clinical trial designed to assess the efficacy and safety of verekitug in participants with severe asthma in extended dosing interval arms of 12 and 24 weeks. Patient enrollment for VALIANT was completed in June 2025. The Company has designed this trial using endpoints that, pending interactions with regulatory authorities, could produce data to support submissions for product approval.

- **Additional program progress:**

- Structural and mechanistic drivers of verekitug's potent pharmacodynamic activity and differentiated clinical profile

were presented at the European Respiratory Society (ERS) Congress in September 2025. Data showed:

- Verekitug prevents TSLP binding to the TSLP receptor by occupying ligand binding sites.
 - Verekitug outcompetes TSLP in the presence of preformed heterodimeric receptor complexes.
 - These data support the potential of verekitug's unique mechanism of action to achieve a differentiated therapeutic effect across a broad range of TSLP-driven severe respiratory diseases.
- Enrollment is ongoing in the VENTURE Phase 2 clinical trial in COPD, in which the first patient was dosed in July 2025. VENTURE is a Phase 2 global, randomized, double-blind, placebo-controlled, parallel group clinical trial designed to assess the efficacy and safety of verekitug in participants with moderate-to-severe COPD in extended dosing interval arms of 12 and 24 weeks. The Company has designed this trial using endpoints that, pending interactions with regulatory authorities, could produce data to support submissions for product approval.

Third Quarter 2025 Financial Results

As of September 30, 2025, Upstream Bio had cash, cash equivalents and short-term investments of \$372.4 million, which is expected to fund planned operations through 2027.

Research and development expenses were \$33.0 million for the quarter ended September 30, 2025, compared to \$15.4 million for the same period in 2024. The increase of \$17.6 million was primarily driven by an increase in clinical and manufacturing expenses related to the Company's verekitug programs.

General and administrative expenses were \$5.5 million for the quarter ended September 30, 2025, compared to \$4.1 million for the same period in 2024. The increase of \$1.4 million was primarily driven by an increase in personnel-related expenses, including share-based compensation, and professional service fees.

Net loss was \$33.7 million for the quarter ended September 30, 2025, compared to a net loss of \$16.0 million for the same period in 2024. The increase of \$17.7 million was largely due to increased research and development expenses.

Upcoming Events

Upstream Bio expects to participate in the following upcoming investor conferences:

- 2025 Truist Securities Biopharma Symposium, November 6, 2025, New York, NY
- Stifel 2025 Healthcare Conference, November 11, 2025, New York, NY
- TD Cowen Immunology and Inflammation Summit, November 12, 2025, Virtual
- Piper Sandler 37th Annual Healthcare Conference, December 2, 2025, New York, NY
- 8th Annual Evercore Healthcare Conference, December 4, 2025, Miami, FL
- 44th Annual J.P. Morgan Healthcare Conference, January 12-15, 2026, San Francisco, CA

About Upstream Bio

Upstream Bio is a clinical-stage biotechnology company developing treatments for inflammatory diseases, with an initial focus on severe respiratory disorders. The Company is developing verekitug, the only known antagonist currently in clinical development that targets and inhibits the receptor for thymic stromal lymphopoietin (TSLP), 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. The Company has advanced this highly potent monoclonal antibody into separate Phase 2 trials for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP), severe asthma, and chronic obstructive pulmonary disease (COPD). 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 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 differentiation, safety, efficacy, tolerability, or extended dosing interval 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.

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UPSTREAM BIO, INC.
CONDENSED CONSOLIDATED BALANCE SHEET
(IN THOUSANDS)
(UNAUDITED)

| | <u>September 30,</u> | <u>December 31,</u> |
|---|----------------------|---------------------|
| | <u>2025</u> | <u>2024</u> |
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | \$ 72,164 | \$ 325,892 |
| Short-term investments | 300,263 | 144,559 |
| Accounts receivable | 683 | 613 |
| Prepaid expenses and other current assets | 15,907 | 8,096 |
| Total current assets | <u>389,017</u> | <u>479,160</u> |
| Property and equipment, net | 616 | 582 |
| Operating lease right-of-use assets | 1,368 | 1,783 |
| Restricted cash | 194 | 194 |
| Total assets | <u>\$ 391,195</u> | <u>\$ 481,719</u> |
| Liabilities and Stockholders' Equity | | |
| Current liabilities: | | |
| Accounts payable | \$ 3,952 | \$ 4,041 |
| Accrued expenses and other current liabilities | 7,240 | 5,992 |
| Operating lease liabilities, current portion | 716 | 704 |
| Total current liabilities | <u>11,908</u> | <u>10,737</u> |
| Operating lease liabilities, net of current portion | 703 | 1,130 |
| Total liabilities | <u>12,611</u> | <u>11,867</u> |
| Stockholders' equity: | | |
| Common stock | 56 | 53 |
| Additional paid-in capital | 669,799 | 660,604 |
| Accumulated other comprehensive income (loss) | 493 | (25) |
| Accumulated deficit | (291,764) | (190,780) |
| Total stockholders' equity | <u>378,584</u> | <u>469,852</u> |
| Total liabilities and stockholders' equity | <u>\$ 391,195</u> | <u>\$ 481,719</u> |

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

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|--|-------------------------------------|--------------------|------------------------------------|--------------------|
| | 2025 | 2024 | 2025 | 2024 |
| Collaboration revenue | \$ 683 | \$ 607 | \$ 2,186 | \$ 1,757 |
| Operating expenses: | | | | |
| Research and development | 32,975 | 15,433 | 96,637 | 41,193 |
| General and administrative | 5,542 | 4,067 | 19,743 | 12,010 |
| Total operating expenses | <u>38,517</u> | <u>19,500</u> | <u>116,380</u> | <u>53,203</u> |
| Loss from operations | <u>(37,834)</u> | <u>(18,893)</u> | <u>(114,194)</u> | <u>(51,446)</u> |
| Other income (expense): | | | | |
| Change in fair value of preferred stock tranche right liability | — | — | — | 2,859 |
| Interest income | 4,105 | 2,904 | 13,279 | 7,047 |
| Other expense, net | (19) | (3) | (69) | (24) |
| Total other income, net | <u>4,086</u> | <u>2,901</u> | <u>13,210</u> | <u>9,882</u> |
| Net loss | <u>\$ (33,748)</u> | <u>\$ (15,992)</u> | <u>\$ (100,984)</u> | <u>\$ (41,564)</u> |