



Upstream Bio Highlights Phase 3 Development Strategy for Verekitug and Reports Fourth Quarter and Full Year 2025 Financial Results

March 26, 2026

- Company to pursue Phase 3 development strategy designed to deliver best-in-class efficacy with a high-dose quarterly regimen in broad patient populations in both severe asthma and CRSwNP –
- Company plans to initiate dosing in Phase 3 trials in both severe asthma and CRSwNP in Q1 2027 –
- Reported positive top-line results from Phase 2 VALIANT trial of verekitug in patients with severe asthma in February 2026, demonstrating significant improvements in asthma exacerbations and lung function –
- Presented additional analyses from Phase 2 VIBRANT trial at AAAAI, reinforcing verekitug's therapeutic potential in CRSwNP –
- Strong cash position of \$341.5 million expected to fund planned operations through 2027 –

WALTHAM, Mass., March 26, 2026 (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 fourth quarter and full year ended December 31, 2025, and highlighted its Phase 3 development strategy for verekitug in severe asthma and chronic rhinosinusitis with nasal polyps (CRSwNP). 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 severe asthma, CRSwNP, and chronic obstructive pulmonary disease (COPD).

"Upstream Bio continues to make strong progress, highlighted by our recent positive Phase 2 VALIANT study of verekitug in patients with severe asthma," said Rand Sutherland, MD, Chief Executive Officer of Upstream Bio. "This trial demonstrated compelling efficacy data and a favorable safety profile with extended dosing, and we believe this combination could represent a meaningful advance over currently available biologic therapies. We are working diligently to move verekitug into Phase 3 development and to realize its potential to become a leading medicine for the treatment of severe asthma and CRSwNP."

"Since reporting the top-line results from VALIANT, we have analyzed data from approximately 500 participants treated in our Phase 1 and 2 clinical trials, and this comprehensive dataset supports verekitug's potential to deliver best-in-class efficacy with doses as high as 400 mg administered quarterly in a single injection, in both severe asthma and CRSwNP," continued Dr. Sutherland. "As a result of this work and comprehensive market research indicating that a profile that delivers best-in-class efficacy with quarterly dosing maximizes the potential commercial value of verekitug, we are prioritizing a Phase 3 development strategy that focuses on maximizing efficacy in both indications, without biomarker restriction, while also delivering the convenience of quarterly at-home administration. We will provide additional details on the study design following engagement with the U.S. Food and Drug Administration (FDA) later this year, and we plan to initiate dosing in both Phase 3 programs in the first quarter of 2027."

Recent Business Highlights

- **Phase 3 Strategy for High-Dose Quarterly Administration in Broad Patient Populations in Severe Asthma and CRSwNP Supported by Analyses of Phase 2 Trial Results**
 - Evaluation of exposure-response relationships across multiple clinical endpoints in both severe asthma and CRSwNP supports the Company's intent to study a high-dose quarterly regimen of verekitug of up to 400 mg, administered in a single injection.
 - As observed in Phase 2 trials, patients in the highest exposure group consistently demonstrated the highest clinical benefit in both severe asthma, as measured by forced expiratory volume in 1 second (FEV₁), and CRSwNP, as measured by the nasal congestion score (NCS) after treatment with 100 mg every 12 weeks.
 - Pharmacokinetic (PK) modeling from all patients treated with verekitug indicates that, at doses above 100 mg every 12 weeks, 85% to 96% of patients at 200 mg every 12 weeks and 400 mg every 12 weeks, respectively, are predicted to have verekitug concentrations sufficient to achieve near-maximal suppression of exhaled nitric oxide throughout the quarterly dosing interval.
 - Observed positive treatment responses across both high and low eosinophil subgroups in severe asthma and CRSwNP reinforce verekitug's continued development in a broad population of patients in both indications.
 - Immunogenicity in Phase 2 trials was consistent with previous experience, and meaningful differences in either safety or efficacy were not observed in patients with anti-drug antibodies as compared to those without.
 - The Company's market research, conducted with healthcare providers, payers, and patients, consistently indicates that efficacy is the primary driver of clinical impact and commercial success in severe asthma and CRSwNP, that healthcare providers are unwilling to trade off any aspect of safety or efficacy for extended dosing, and that the

majority of value generated by dosing convenience is captured by moving from every 2- or 4-week dosing to quarterly dosing. These findings support the Company's development strategy focused on delivering high efficacy with quarterly dosing convenience.

- o The Company plans to meet with regulators later this year to gain alignment on Phase 3 plans for verekitug in severe asthma and CRSwNP and expects to initiate both registrational studies in the first quarter of 2027.

- **Positive Phase 2 VALIANT Trial in Severe Asthma Results Reported**

- o Top-line results from the Phase 2 VALIANT trial in severe asthma [reported in February 2026](#) demonstrated significant improvements in asthma exacerbations and lung function with extended dosing.
- o In this randomized, placebo-controlled study, VALIANT met the study's primary endpoint of a statistically significant and clinically meaningful reduction in the annualized asthma exacerbation rate (AAER) with both every 12 week and every 24 week dosing, with verekitug demonstrating a reduction in AAER of 56% ($p < 0.0003$) when dosed at 100 mg every 12 weeks and 39% ($p < 0.02$) when dosed at 400 mg every 24 weeks, as compared with placebo.
- o Verekitug demonstrated a favorable safety profile across all doses tested, consistent with previous studies.

- **Additional Analyses of Phase 2 VIBRANT Trial in CRSwNP Presented at 2026 American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting**

- o Upstream Bio [presented additional analyses](#) from the Phase 2 VIBRANT trial of verekitug in patients with CRSwNP at the AAAAI Annual Meeting in February 2026. The analyses further characterized the efficacy and safety profile of verekitug, including evaluations adjusting for the use of rescue therapies, supporting the previously reported significant and clinically meaningful reductions in nasal polyp burden and symptom measures.
 - Dosed 100 mg every 12 weeks, verekitug met the study's primary endpoint using both the worst-observation carried-forward (WOCF) and primary (treatment policy) analyses, demonstrating a larger placebo-adjusted reduction in nasal polyp score (NPS) of -1.95 ($p < 0.0001$) in the WOCF analysis as compared to a reduction of -1.77 ($p < 0.0001$) in the primary analysis at week 24.
 - The trial also showed a placebo-adjusted reduction in the patient-reported NCS, a key secondary endpoint, of -0.96 ($p < 0.0001$) in the WOCF analysis as compared to -0.77 ($p = 0.0003$) in the primary analysis.
- o These findings provide additional support for the continued development of verekitug and ongoing planning for Phase 3 registrational studies.

- **Ongoing Enrollment of Phase 2 VENTURE Trial in COPD**

- o Enrollment is ongoing in the Phase 2 VENTURE clinical trial in COPD ([NCT06981078](#)), which was initiated 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 across 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. The VENTURE study is more than 60% enrolled.

Fourth Quarter 2025 Financial Results

As of December 31, 2025, Upstream Bio had cash, cash equivalents and short-term investments of \$341.5 million, which is expected to fund planned operations through 2027.

Research and development expenses were \$40.2 million for the quarter ended December 31, 2025, compared to \$21.8 million for the same period in 2024. The increase of \$18.4 million was primarily driven by an increase in clinical and manufacturing expenses related to the Company's verekitug programs.

General and administrative expenses were \$6.7 million for the quarter ended December 31, 2025, compared to \$5.2 million for the same period in 2024. The increase of \$1.5 million was primarily driven by an increase in professional fees and personnel-related expenses, including share-based compensation.

Net loss was \$42.5 million for the quarter ended December 31, 2025, compared to a net loss of \$21.2 million for the same period in 2024. The increase of \$21.3 million was largely due to increased research and development expenses.

Upcoming Events

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

- Piper Sandler Spring Biopharma Symposium, April 15-16, Boston, MA
- American Thoracic Society 2026 International Conference, May 15-20, Orlando, FL
- Goldman Sachs 47th Annual Global Healthcare Conference, June 8-10, Miami, FL
- European Academy of Allergy & Clinical Immunology, June 12-16, Istanbul, Turkey

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 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 differentiation, safety, efficacy, tolerability, or extended dosing interval of verekitug; expectations for the size and growth potential of the market for verekitug and the Company's ability to serve that market; certain activities and next steps to support the Company's maturation into a late clinical-stage company; expectations regarding the planned regulatory interactions with the FDA on the data from the VIBRANT and VALIANT Phase 2 trials and the outcomes of any such interactions; 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 results of preclinical studies or clinical studies not being predictive of future results in connection with future studies; 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:

Meggan Buckwell
 Director, Corporate Communications and Investor Relations
ir@upstreambio.com

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

	<u>December 31,</u> <u>2025</u>	<u>December 31,</u> <u>2024</u>
Assets		
Current assets:		
Cash and cash equivalents	\$ 101,578	\$ 325,892
Short-term investments	239,931	144,559
Accounts receivable	668	613

Prepaid expenses and other current assets	9,620	8,096
Total current assets	351,797	479,160
Property and equipment, net	559	582
Operating lease right-of-use assets	1,222	1,783
Restricted cash	194	194
Total assets	<u>\$ 353,772</u>	<u>\$ 481,719</u>
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 2,726	\$ 4,041
Accrued expenses and other current liabilities	10,006	5,992
Operating lease liabilities, current portion	720	704
Total current liabilities	13,452	10,737
Operating lease liabilities, net of current portion	549	1,130
Total liabilities	14,001	11,867
Stockholders' equity:		
Common stock	54	53
Additional paid-in capital	673,410	660,604
Accumulated other comprehensive income (loss)	530	(25)
Accumulated deficit	(334,223)	(190,780)
Total stockholders' equity	339,771	469,852
Total liabilities and stockholders' equity	<u>\$ 353,772</u>	<u>\$ 481,719</u>

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

	Three Months Ended December 31,		Years Ended December 31,	
	2025	2024	2025	2024
Collaboration revenue	\$ 668	\$ 613	\$ 2,854	\$ 2,370
Operating expenses:				
Research and development	40,169	21,773	136,806	62,966
General and administrative	6,666	5,158	26,409	17,168
Total operating expenses	46,835	26,931	163,215	80,134
Loss from operations	(46,167)	(26,318)	(160,361)	(77,764)
Other income (expense):				
Change in fair value of preferred stock tranche right liability	—	—	—	2,859
Interest income	3,654	5,076	16,933	12,123
Other income (expense), net	54	—	(15)	(24)
Total other income, net	3,708	5,076	16,918	14,958
Net loss	<u>\$ (42,459)</u>	<u>\$ (21,242)</u>	<u>\$ (143,443)</u>	<u>\$ (62,806)</u>