Upstream Bio Presents Results from the Phase 2 VALIANT Trial of Verekitug for the Treatment of Severe Asthma in Oral Presentation at ERS Congress 2026

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– Verekitug, 100 mg dosed every 12 weeks, reduced AAER by 56% compared to placebo in patients with severe asthma –

– Verekitug also delivered clinically meaningful improvements in lung function (FEV_1) and exhaled nitric oxide (FeNO) with every 12-week dosing –

– The Company remains on track to initiate Phase 3 trials in severe asthma and CRSwNP in Q1 2027, designed to deliver best-in-class efficacy in both indications by evaluating a 400 mg quarterly regimen of verekitug in broad patient populations –

WALTHAM, Mass., Sept. 08, 2026 (GLOBE NEWSWIRE) -- Upstream Bio, Inc. (Nasdaq: UPB), a clinical-stage company developing treatments for severe inflammatory respiratory diseases, today presented results from the Phase 2 VALIANT clinical trial evaluating the safety and efficacy of verekitug in adults with severe asthma in a late-breaking oral presentation at the European Respiratory Society (ERS) Congress 2026 in Barcelona. Verekitug is the only known antagonist currently in clinical development that targets and inhibits the thymic stromal lymphopoietin (TSLP) receptor.

As previously reported, VALIANT met the study's primary endpoint of a statistically significant and clinically meaningful reduction in the annualized asthma exacerbation rate (AAER) across all dose regimens studied. Verekitug, 100 mg dosed every 12 weeks, reduced AAER by 56% ($p<0.001$) compared to placebo. Statistically significant reductions in AAER were also observed in the two other dose arms.

"We are excited to share results of the Phase 2 VALIANT study, which demonstrate that treatment with verekitug led to significant and substantial improvements in asthma exacerbations, lung function and inflammatory biomarkers, at this year's ERS Congress," said Aaron Deykin, MD, Chief Medical Officer and Head of Research & Development at Upstream Bio. "The compelling efficacy profile, highlighted by a 56% reduction in AAER observed in patients receiving verekitug every 12 weeks, together with the favorable safety results, reinforces the potential of targeting the TSLP receptor to potently address key measures of disease. These findings, part of the dataset from more than 500 trial participants treated with verekitug to date, further strengthen our conviction in verekitug's potential to deliver best-in-class efficacy with the convenience of quarterly dosing, a profile we plan to further evaluate in a broad severe asthma population in Phase 3."

"Despite the availability of effective biologic therapies, there continues to be a need for treatments that can provide meaningful disease control while reducing patient burden," said Michael Wechsler, MD, MMSc, Professor of Medicine, Director of National Jewish Cohen Family Asthma Institute and principal investigator on the VALIANT trial. "The consistency and magnitude of improvement observed with verekitug in the VALIANT study suggests it has the potential to deliver meaningful clinical benefit for people living with severe asthma. The substantial reduction in asthma exacerbations, together with improvements across multiple measures of disease activity including lung function, demonstrate verekitug's potential to achieve strong disease control with infrequent dosing. These results support its continued development as an important potential treatment option for severe asthma."

VALIANT (NCT06196879) is a Phase 2 global, randomized, double-blind, placebo-controlled, dose-ranging, parallel group clinical trial that evaluated the safety and efficacy of verekitug in 478 patients with severe asthma. Patients were enrolled regardless of baseline blood eosinophil count or other type-2 biomarker levels. The trial was designed with a variable treatment period with all participants having at least 24 weeks of treatment and those enrolled prior to the last randomized participant having additional treatment up to a maximum of 60 weeks.

Verekitug improved the key secondary outcomes of FEV_1 (forced expiratory volume in one second), FeNO (fractional exhaled nitric oxide), and asthma symptom control as measured by Asthma Control Questionnaire (ACQ-6) versus placebo at week 24, with improvements seen as early as week 2 across all key secondary outcomes.

Verekitug was generally well tolerated across all active doses, demonstrating a favorable safety profile consistent with previous studies. Immunogenicity had no meaningful impact on safety or efficacy results.

Eligible participants who completed the Phase 2 VALIANT clinical trial were offered enrollment in VALOUR (NCT06966479), a long-term extension (LTE) study designed to evaluate the long-term safety and efficacy of verekitug. VALOUR completed enrollment in March 2026 with more than 90% retention of eligible patients from the Phase 2 VALIANT study, with data expected in the second half of 2027.

As previously announced, Upstream Bio remains on track to initiate Phase 3 clinical trials with verekitug administered every 12 weeks in severe asthma and CRSwNP in the first quarter of 2027. The Phase 3 trials will evaluate 400 mg of verekitug

administered every 12 weeks, versus placebo, with the goal to deliver best-in-class efficacy with quarterly at-home administration for patients with severe asthma and CRSwNP, in broad study populations without restriction based on baseline biomarkers.

A digital version of the presentation and e-poster can be found on the Publications section of the Upstream Bio website.

About Verekitug
Verekitug is a novel recombinant fully human immunoglobulin G1 (IgG1) monoclonal antibody that binds to the thymic stromal lymphopoietin (TSLP) receptor and inhibits proinflammatory signaling initiated by TSLP. It is the only known antagonist currently in clinical development that targets and inhibits the TSLP receptor.

TSLP is a cytokine that is a key driver of the inflammatory response in major allergic and inflammatory diseases, such as asthma, where disruption of TSLP signaling has been clinically validated as an effective therapeutic strategy. TSLP activation is one of the first events in the inflammatory cascade stimulated by allergens, viruses and other triggers, initiating the activation of downstream targets such as IL-4, IL-5, IL-13, IL-17 and IgE. Because TSLP is a target upstream in the inflammatory cascade, blocking the TSLP receptor presents an opportunity for a single treatment to impact the drivers of multiple pathological inflammatory processes across a broad set of diseases.

With more than 500 participants treated with verekitug across its clinical development programs and positive Phase 2 results in severe asthma and chronic rhinosinusitis with nasal polyps (CRSwNP), verekitug has a substantial body of clinical evidence supporting its advancement into Phase 3 development in both diseases. Verekitug is also being evaluated in an ongoing Phase 2 trial in chronic obstructive pulmonary disease (COPD).

About Upstream Bio
Upstream Bio is a clinical-stage biotechnology company developing treatments for severe inflammatory respiratory diseases. 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 inflammatory pathways. With more than 500 participants treated with verekitug across its clinical development programs and positive Phase 2 results in chronic rhinosinusitis with nasal polyps (CRSwNP) and severe asthma, verekitug has a substantial body of clinical evidence supporting its advancement into Phase 3 development in both diseases. Verekitug is also being evaluated in an ongoing Phase 2 trial in chronic obstructive pulmonary disease (COPD). Upstream Bio is focused on leveraging verekitug's differentiated mechanism, potency, and potential for extended dosing to develop a treatment which may deliver best-in-class efficacy and quarterly dosing for patients underserved by today's standard of care.

To learn more, please visit www.upstreambio.com.

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 Company's plans to initiate Phase 3 clinical trials in severe asthma and CRSwNP in the first quarter of 2027 and the timing, progress and results of ongoing and planned clinical trials; expectations regarding the potential of verekitug to deliver best-in-class efficacy and its differentiation, safety, and tolerability; and expectations regarding regulatory interactions with the U.S. Food and Drug Administration, including the Company's Phase 3 clinical development plans in severe asthma and CRSwNP and the outcomes of any such interactions. 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, including any additional interactions with the FDA regarding the sufficiency of Upstream Bio's Phase 3 development plans; 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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