Upstream Bio Reports Positive Top-line Results from the Phase 2 VALIANT Trial of Verekitug for the Treatment of Severe Asthma

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– Verekitug provided statistically significant and clinically meaningful reductions in annualized asthma exacerbation rate (AAER) with 100 mg q12 and 400 mg q24 week dosing –

– Verekitug also delivered clinically meaningful improvements in lung function (FEV_1) and exhaled nitric oxide (FeNO) with both dose regimens –

– Verekitug was generally well tolerated, with a safety profile consistent with prior studies –

– Over 90% of eligible patients have rolled over to the Phase 2 VALOUR long-term extension study –

– Upstream Bio to advance verekitug into Phase 3 trials in severe asthma and CRSwNP following planned regulatory interactions –

– Management will host a live webcast today at 8:00 a.m. ET –

WALTHAM, Mass., Feb. 11, 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 announced positive top-line results from the Phase 2 VALIANT clinical trial evaluating the safety and efficacy of verekitug in adults with severe asthma. Verekitug is the only known clinical-stage antagonist targeting the receptor for thymic stromal lymphopoietin (TSLP).

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 (q12w) and every 24 week (q24w) dosing, with verekitug demonstrating a reduction in AAER of 56% ($p<0.0003$) when dosed at 100 mg q12w and 39% ($p<0.02$) when dosed at 400 mg q24w, as compared with placebo.

Placebo-adjusted improvement in lung function, as measured by the forced expiratory volume in one second (FEV_1), was 122 mL at week 60 with verekitug 100 mg q12w, and 139 mL at week 60 with 400 mg q24w. At week 60, verekitug also suppressed exhaled nitric oxide (FeNO) compared to placebo by 20.4 ppb ($p<0.0003$) when dosed at 100 mg q12w, and by 26.3 ppb ($p<0.0001$) when dosed at 400 mg q24w. These data represented a mean 43.5% ($p=0.03$) reduction from baseline in the 100 mg q12w group and a mean 44.9% ($p=0.03$) reduction from baseline in the 400 mg q24w group. A third low-dose treatment group, 100 mg q24w, demonstrated a statistically significant effect on AAER, but did not provide consistent improvements in other endpoints.

Additional pre-specified analyses of secondary outcomes at week 24 revealed statistically significant placebo-adjusted improvements compared to baseline in both FEV_1 and FeNO with the 100 mg q12w and 400 mg q24w dose regimens.

Verekitug was generally well tolerated across all active doses, demonstrating a favorable safety profile consistent with previous studies.

"We are excited to share these robust data from VALIANT, which indicate the potential of verekitug's meaningful clinical effect in severe asthma and provide a strong foundation as we advance verekitug into Phase 3 clinical trials as quickly as possible," said Aaron Deykin, MD, Chief Medical Officer and Head of Research & Development at Upstream Bio. "We are deeply grateful to the patients, investigators, and study teams whose participation made this progress possible. With the completion of our VALIANT trial, hundreds of patients have now been dosed with verekitug across our clinical programs, providing a growing body of clinical experience that reinforces our confidence in its potential and its differentiated product profile. Together with the positive results from our VIBRANT trial in CRSwNP, we now have an opportunity to incorporate both strong clinical data sets with an in-depth analysis of the aggregate pharmacology findings to guide data-driven decisions about dose selection and trial design for Phase 3."

"These compelling findings from VALIANT strengthen verekitug's potential to advance the standard of care with a highly competitive efficacy profile and less frequent dosing—an important combination for people living with severe asthma," stated Rand Sutherland, MD, Chief Executive Officer of Upstream Bio. "We intend to rapidly advance verekitug into Phase 3 trials in severe asthma and CRSwNP. In parallel, we also continue to progress verekitug in our ongoing Phase 2 VENTURE trial in patients with COPD, where we have enrolled more than 60% of patients to date. As we transition into a late clinical-stage company pursuing substantial market opportunities, our focus remains on disciplined execution and expanding Upstream Bio's capabilities to support long-term growth."

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 for up to 60 weeks, with a minimum of 24 weeks of treatment, in 478 patients with severe asthma.

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. Current transition rates indicate more than 90% of eligible patients have rolled over to the Phase 2 VALOUR LTE study.

"Severe asthma, when unable to be controlled by standard of care measures, can significantly and chronically disrupt patients' quality of life, and put them at risk for potentially life-threatening exacerbation events that can lead to emergency rooms visits and hospitalizations," said Michael Wechsler, MD, MMSc, Professor of Medicine, Director of National Jewish Cohen Family Asthma Institute. "These data suggest that verekitug can potentially offer patients meaningful improvements in their breathing and asthma symptoms with less frequent dosing than the currently available biologics, and I believe that verekitug could represent an important advancement for individuals living with severe asthma."

Upstream Bio designed the VALIANT trial using endpoints that, pending interactions with regulatory authorities, could produce data to support submissions for product approval. Planning activities for Phase 3 trials in severe asthma and CRSwNP have commenced, and the Company intends to initiate registrational trials in both indications following planned regulatory interactions.

Additional details from the VALIANT trial will be presented at a future medical conference.

Webcast Details
Upstream Bio's webcast to discuss the top-line results from the Phase 2 VALIANT trial will begin today at 8:00 a.m. ET. The live webcast can be accessed via this link or on the Events tab on the Investors section of the Company's website at https://investors.upstreambio.com/news-events/events. A replay of the webcast will be available on the website following the call.

About Severe Asthma
Severe asthma is a complex, chronic inflammatory disease of the airways characterized by persistent symptoms, recurrent exacerbations, and impaired quality of life despite treatment with high-dose corticosteroids and other long-acting medication that accounts for a disproportionate share of asthma-related costs and healthcare utilization. Severe asthma is a heterogeneous disease driven by multiple inflammatory pathways, including both Type 2 and non-Type 2 mechanisms.

Asthma affects approximately 350 million people worldwide, with five to 10 percent suffering from severe asthma. Currently, there are approximately 1.3 million biologic-eligible severe asthma patients in the US, though the use of biologic therapies remains limited relative to the size of the eligible population. We believe new treatment options for severe asthma are needed to further improve control of exacerbations and symptoms, and reduce the treatment burden, such as the need for frequent injections.

About the Phase 2 VALIANT Trial
The Phase 2 VALIANT trial (NCT06196879) is a global, randomized, placebo-controlled, dose-finding, parallel group clinical trial, designed to assess the efficacy and safety of verekitug in adults with severe asthma. Participants were randomized into one of four groups, receiving either 100 mg of verekitug every 24 weeks, 400 mg of verekitug every 24 weeks, 100 mg of verekitug every 12 weeks, or placebo administered subcutaneously. The study evaluated verekitug's efficacy in the treatment of severe asthma during a treatment period up to 60 weeks with a minimum of 24 weeks, with the primary endpoint of reduction of the annualized asthma exacerbation rate (AAER). Secondary endpoints included changes in air exhalation, nitric oxide exhalation, and a patient-reported assessment of asthma control, though these were not designed with sufficient power to detect statistically significant effects.

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.

Verekitug has advanced into three separate global, placebo-controlled, randomized Phase 2 clinical trials including the recently completed positive VIBRANT trial (NCT06164704) in patients with CRSwNP and VALIANT trial (NCT06196879) in patients with severe asthma. The VENTURE trial (NCT06981078) in patients with moderate-to-severe chronic obstructive pulmonary disease (COPD) is ongoing. Additionally, in May 2025, Upstream Bio initiated the VALOUR trial (NCT06966479), a long-term extension study in eligible participants with severe asthma who completed the VALIANT Phase 2 clinical trial.

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 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.

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; 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; 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.

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