Upstream Bio Presents Additional Analyses from the Phase 2 VIBRANT Trial of Verekitug in Chronic Rhinosinusitis with Nasal Polyps at 2026 AAAAI Annual Meeting

March 1, 2026

– Primary endpoint of endoscopic nasal polyp score (NPS) showed reduction of -1.95 (p < 0.0001) in new analysis with adjustment for concomitant rescue therapy use –

– Secondary endpoints also provided strong efficacy data in new analyses, including reduction in nasal congestion score (NCS) by -0.96 (p < 0.0001) –

WALTHAM, Mass., March 01, 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 presented additional data from the Phase 2 VIBRANT clinical trial evaluating verekitug in participants with chronic rhinosinusitis with nasal polyps (CRSwNP). The additional analyses incorporated a worst-observation carried-forward (WOCF) statistical approach to adjust for concomitant rescue therapy use, including nasal polyp surgery, systemic corticosteroids, or escalation of background treatments. The data support previously reported positive top-line results and were presented in a late-breaking poster session at the American Academy of Allergy Asthma & Immunology (AAAAI) 2026 Annual Meeting in Philadelphia.

Dosed 100 mg every 12 weeks, verekitug met the study's primary endpoint using both the WOCF and primary (treatment policy) analyses, demonstrating an improved placebo-adjusted reduction in 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.

As previously reported in the top-line results, verekitug reduced the need for surgery or systemic corticosteroids by 76% (p = 0.03) compared with placebo, and was generally well tolerated, demonstrating a favorable safety profile consistent with previous studies, with no SAEs observed.

"The strong results in clinical effect we saw in these additional analyses are an important validation of verekitug's impact on endpoints that take into consideration the use of rescue medication, which was substantially reduced with verekitug treatment in VIBRANT. As this approach more closely aligns with that used in other recent studies of agents in CRSwNP, it also enhances our understanding of verekitug's potential to add to the existing armamentarium for this serious disease. The presentation of these data continues to reinforce verekitug's differentiated profile, comprising robust clinical activity with far less-frequent dosing, relative to currently available biologics as a potential treatment of CRSwNP," said Aaron Deykin, MD, Chief Medical Officer and Head of Research & Development at Upstream Bio. "As we prepare to initiate our Phase 3 trials in CRSwNP and severe asthma, we believe that verekitug's unique mechanism of action and differentiated product profile could position it to significantly advance the standard of care for people with serious respiratory diseases."

"The magnitude of improvement observed with verekitug across both analytical approaches, along with the previously reported reduction in rescue interventions, suggests the potential for meaningful benefit for people living with chronic rhinosinusitis with nasal polyps," said Joseph Han, MD, Professor in the Department of Otolaryngology & Head and Neck Surgery and the Chief for the Division of Allergy at Old Dominion University (Eastern Virginia Medical School), and principal investigator on the VIBRANT trial. "Additionally, the efficacy outcomes we observed in VIBRANT, combined with the every 12-week dosing interval, suggest that verekitug could represent a valuable new treatment option for people living with this challenging condition."

VIBRANT (NCT06164704) was a Phase 2 global, randomized, double-blind, placebo-controlled, parallel group clinical trial that evaluated the efficacy and safety of verekitug over 24 weeks in 81 adults with CRSwNP.

Upstream Bio designed the VIBRANT 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 CRSwNP and severe asthma have commenced, and the Company intends to initiate registrational trials in both indications, following planned regulatory interactions.

About CRSwNP
CRSwNP is a chronic inflammatory disease of the upper airway, marked by inflammation in the nose and sinuses and the presence of nasal polyps. CRSwNP has four main symptoms: runny nose or postnasal drip, nasal congestion, facial pressure and/or pain and loss of smell and/or taste. Despite available treatments such as corticosteroids, surgery and, more recently, biologics, the quality-of-life studies and post-surgical recurrence rates clearly show that many people with CRSwNP have uncontrolled symptoms that are impacting their daily life and current treatments are not meeting their needs. It is estimated that

CRSwNP affects up to 4% of the general population, of whom 40% have uncontrolled disease.

Nasal polyps are associated with significant disease burden and debilitating symptoms; it is estimated that over 40% of people with severe asthma also have CRSwNP and that up to 70% of people with CRSwNP also have asthma, demonstrating a strong association between the two conditions.

About the Phase 2 VIBRANT Trial
The Phase 2 VIBRANT trial (NCT06164704) was a global, randomized, placebo-controlled, parallel group clinical trial, which was designed to assess the efficacy and safety of verekitug in adults with CRSwNP who were receiving concurrent intranasal corticosteroid therapy. Participants received either 100 mg of verekitug or placebo subcutaneously every 12 weeks for 24 weeks. The primary endpoint was change in endoscopic nasal polyp score at Week 24, a primary endpoint that has been used in several registrational trials for other biologic treatments for CRSwNP. Secondary endpoints included: nasal congestion score, sinus opacification, difficulty with sense of smell, total symptom score, percentage of participants requiring systemic corticosteroids or nasal polyp surgery, and time to first such interventions up to Week 24.

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 evaluated this highly potent monoclonal antibody in separate Phase 2 trials for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP), severe asthma, and an ongoing Phase 2 trial in 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 global 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, and/or extended dosing interval of verekitug; and expectations for the size and growth potential of the market for verekitug in CRSwNP and the Company's ability to serve that market. 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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