Upstream Bio Reports Positive Top-Line Results from the Phase 2 VIBRANT Trial of Verekitug for the Treatment of Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

September 2, 2025

– 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) –

– 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 –

– No serious adverse events (SAEs) observed; generally well tolerated safety profile consistent with previous studies –

– 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 –

– Management will host a conference call and webcast today at 8:00 a.m. ET –

WALTHAM, Mass., Sept. 02, 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 announced positive top-line results from the Phase 2 VIBRANT trial evaluating verekitug in participants with chronic rhinosinusitis with nasal polyps (CRSwNP). Verekitug is the only known clinical-stage monoclonal antibody targeting the receptor for thymic stromal lymphopoietin (TSLP).

Over the 24-week treatment period, verekitug, dosed 100mg every 12 weeks, met the primary endpoint and key secondary endpoints, demonstrating statistically significant and clinically meaningful reductions in both endoscopic nasal polyp score (NPS) and nasal congestion score (NCS), with a generally well tolerated safety profile consistent with previous studies. Treatment with verekitug also resulted in a significant reduction in the need for surgery or systemic corticosteroids.

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.

The trial met its primary endpoint, demonstrating a statistically significant and clinically meaningful, placebo-adjusted reduction in NPS of -1.8 (p<0.0001) at Week 24 compared with baseline. The trial also showed a meaningful placebo-adjusted reduction from baseline in the patient-reported NCS, a key secondary endpoint, by -0.8 (p=0.0003).

Significant improvements were also observed in other key secondary endpoints, including sinus opacification as measured by the Lund-Mackay score, reduction in the need for either systemic corticosteroids or nasal polyp surgery, and total symptom score (TSS).

Verekitug was generally well tolerated, demonstrating a favorable safety profile consistent with previous studies, with no SAEs observed.

“This is an important milestone in the development of verekitug. The VIBRANT trial results demonstrated statistically significant and clinically meaningful benefits with verekitug dosed every 12 weeks, positioning it to potentially advance the standard of care in the treatment of CRSwNP,” said Aaron Deykin, MD, Chief Medical Officer and Head of Research & Development at Upstream Bio. “These results reinforce our earlier observations that verekitug’s high potency, achieved through targeting the TSLP receptor, has the potential to translate into clinical attributes distinct from those offered by any currently available therapy.”

“These results highlight verekitug’s distinctive profile: significant clinical effect and extended dosing, driven by potency related to the unique mechanism of action. We believe that verekitug has the potential to be an important addition to existing biologic options for the treatment of CRSwNP, a disease where there remains substantial unaddressed clinical need,” stated Rand Sutherland, MD, Chief Executive Officer of Upstream Bio. “These results may also offer insight into verekitug’s potential clinical utility in other respiratory diseases, including severe asthma. As we prepare to report top-line data in severe asthma in the coming months, we are encouraged by these findings and remain committed to maximizing the opportunity to transform care with verekitug in multiple indications.”

“In CRSwNP, patients often face persistent nasal obstruction and diminished sense of smell despite repeated courses of systemic corticosteroids or sinus surgery—all of which significantly impact quality of life,” 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. “The improvements observed with verekitug, including durable nasal polyp reduction and symptom relief with a treatment potentially administered only four times per year, are encouraging. These results suggest verekitug could represent a meaningful advancement in the treatment of this chronically debilitating condition.”

Upstream Bio designed the VIBRANT trial using endpoints that, pending interactions with regulatory authorities, could produce data to support submissions for product approval. The Company plans to further engage with global regulatory authorities on the continued development of verekitug.

Upstream Bio plans to present further details from the VIBRANT trial at an upcoming medical conference.

Conference Call and Webcast Details

Upstream Bio’s webcast of the Phase 2 VIBRANT top-line results 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 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 TSLP receptor and inhibits proinflammatory signaling initiated by TSLP. It is the only known monoclonal antibody currently in clinical development that targets and inhibits the TSLP receptor. Verekitug is being evaluated in three separate global, placebo-controlled, randomized Phase 2 clinical trials: the VIBRANT trial (NCT06164704) in patients with chronic rhinosinusitis with nasal polyps (CRSwNP), the VALIANT trial (NCT06196879) in patients with severe asthma, and the VENTURE trial (NCT06981078) in patients with moderate-to-severe chronic obstructive pulmonary disease (COPD). 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.

In preclinical studies, verekitug demonstrated high occupancy of the TSLP receptor and potent inhibition of TSLP signaling. Additionally, verekitug inhibited cytokine production from both CD4+ T cells and ILC2 cells and completely suppressed skin allergic reactions in a non-human primate model, suggesting that it may be effective against multiple types of inflammation.

Three Phase 1 clinical trials have been completed for verekitug, including a Phase 1 single-ascending dose (SAD) clinical trial and a Phase 1b multiple-ascending dose (MAD) clinical trial. In these trials, verekitug was well tolerated, had no clinically meaningful immunogenicity, and showed a predictable and consistent pharmacokinetic profile and high subcutaneous bioavailability. In patients with asthma, verekitug led to >50% reductions in fractional exhaled nitric oxide (FeNO) and blood eosinophils that were rapid and sustained for up to 24 weeks after the last dose in the Phase 1b MAD trial.

About TSLP and TSLPR Blockade
Thymic Stromal Lymphopoietin (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 (TSLPR) presents an opportunity for

a single treatment to impact the drivers of multiple pathological inflammatory processes across a broad set of diseases.

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 in CRSwNP and the Company's ability to serve that market; Upstream Bio's expected operating expenses and capital expenditure requirements; 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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