Upstream Bio Announces Pivotal Phase 3 Development Plans for Verekitug in Both Severe Asthma and CRSwNP

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– Following productive FDA discussions, Upstream Bio will study 400 mg of verekitug administered every 12 weeks, versus placebo, in severe asthma and CRSwNP with one pivotal Phase 3 trial in each indication –

– The Company's Phase 3 strategy is designed to deliver best-in-class efficacy across both indications by evaluating a high-dose, quarterly regimen of verekitug in broad patient populations –

– The Company remains on track to initiate both Phase 3 trials in Q1 2027 –

WALTHAM, Mass., Sept. 01, 2026 (GLOBE NEWSWIRE) -- Upstream Bio, Inc. (Nasdaq: UPB), a clinical-stage company developing treatments for severe inflammatory respiratory diseases, today announced its pivotal Phase 3 development plans for verekitug in severe asthma and chronic rhinosinusitis with nasal polyps (CRSwNP). Verekitug is the only known antagonist currently in clinical development that targets and inhibits the thymic stromal lymphopoietin (TSLP) receptor.

"Following productive End-of-Phase 2 meetings with the U.S. FDA, we are pleased to share our Phase 3 development plans for verekitug and are moving quickly to initiate one placebo-controlled Phase 3 trial each in severe asthma and CRSwNP," said Aaron Deykin, MD, Chief Medical Officer and Head of Research & Development at Upstream Bio. "Leveraging the data from our extensive development program to date, our goal is to deliver best-in-class efficacy with quarterly at-home administration for patients with severe asthma and CRSwNP, irrespective of biomarker status. We plan to evaluate a single high-dose regimen of 400 mg, administered every 12 weeks, in broad and representative patient populations, with the intent to robustly demonstrate verekitug's efficacy and safety profile in these diseases with substantial unmet medical need."

"We are at a pivotal moment in our mission to develop verekitug as a potentially transformative medicine, and we are thrilled to announce plans for our Phase 3 trials in severe asthma and CRSwNP, expected to begin in the first quarter of 2027," said Rand Sutherland, MD, Chief Executive Officer of Upstream Bio. "Our Phase 3 plans for verekitug provide a focused path to further establish its differentiated profile for patients and physicians, with convenient quarterly dosing and the potential for best-in-class efficacy. With clinical trial data from over 500 treated patients and compelling placebo-controlled Phase 2 trials delivering important clinical outcomes, we have a deep understanding of the pharmacology and potential clinical impact of verekitug. We believe we are well positioned to maximize verekitug's clinical and commercial potential as we advance into late-stage development with an efficient Phase 3 strategy across two indications."

Upcoming Initiation of Phase 3 Trials in Severe Asthma and CRSwNP

- The Company plans to execute Phase 3 programs evaluating:
  - A single high-dose subcutaneous regimen of 400 mg administered every 12 weeks;
  - A single placebo-controlled study in each indication enrolling a total of approximately 1,500 patients across both trials;
  - Broad study populations without restriction based on baseline biomarkers;
  - Study primary endpoints:
    - Asthma – Annualized asthma exacerbation rates (AAER) over 48 weeks;
    - CRSwNP – Co-primary endpoints of change from baseline in nasal polyp score (NPS) and in nasal congestion score (NCS) each at 48 weeks.

Upstream Bio remains on track to initiate Phase 3 clinical trials in severe asthma and CRSwNP in the first quarter of 2027. With supportive Phase 3 results, the Company expects to submit a Biologics License Application (BLA) to the FDA for both indications, which could enable potential launch as early as 2030.

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 that 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; the potential to develop verekitug for quarterly at-home administration for patients with severe asthma and CRSwNP, irrespective of biomarker status; expectations regarding regulatory interactions with the FDA, including the Company's Phase 3 clinical development plans in severe asthma and CRSwNP and the outcomes of any such interactions; expectations regarding the commercial potential of verekitug; the timing and submission of regulatory filings, including BLAs, with the FDA; and the potential for U.S. approval and launch of verekitug as early as 2030. 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 FDA 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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