**Upstream Bio Presents Results from a Dose Ranging Study of Verekitug (UPB-101) in Adults with Asthma at the American Thoracic Society International Conference**

*– In a multiple-ascending dose (MAD) study in patients with asthma, up to 54% reduction in fractional exhaled nitric oxide concentration (FENO) was observed with administration of verekitug, with treatment effects sustained up to 24 weeks after last dose –*

*– Verekitug displayed a favorable safety and tolerability profile without evidence of clinically meaningful immunogenicity over 32 weeks –*

*– Data to date support dosing intervals of 12 and 24 weeks in Phase 2 –*

**WALTHAM, Mass. – May 22, 2024** - Upstream Bio, Inc., a clinical-stage company focused on the development of verekitug, a potential first-in-class antagonist of the Thymic Stromal Lymphopoietin (TSLP) receptor that may deliver best-in-class efficacy for people with severe asthma and related diseases, today presented clinical data from its dose-ranging study of verekitug (UPB-101) in adults with asthma, at the American Thoracic Society International Conference being held in San Diego, CA.

In all doses of verekitug, a rapid and complete TSLP receptor (TSLPR) occupancy within 2 weeks after the first dose was observed, and in doses ≥100 mg, TSLPR occupancy was sustained for up to 24 weeks after the last dose. As a result, a substantial reduction of FENO within 2 weeks after the first dose was observed in all doses of verekitug. With 100 mg of verekitug, a 54% reduction of FENO from baseline that was sustained for up to 24 weeks after the last dose was observed. Similar rapid, substantial and sustained reductions were observed in blood eosinophils, a type of white blood cell found in increased numbers in many patients with asthma. FENO is an accepted biomarker for underlying Type 2 lung inflammation in patients with asthma; higher levels of FENO are associated with an increased risk for future asthma exacerbations.

Verekitug was well-tolerated at all dose levels tested; the most common treatment emergent adverse event was headaches.

“These clinical data add to the growing scientific evidence that blocking the TSLPR may be an effective and durable approach to blocking the TSLP signaling pathway driving inflammatory diseases such as severe asthma. The rapid, substantial and sustained reduction in FENO and blood eosinophils observed for up to 24 weeks supports verekitug’s potential to deliver significant beneficial effects on clinical outcomes with potential administration every 12 or 24 weeks,” said Aaron Deykin, M.D., Upstream Bio's Chief Medical Officer and Head of R&D.

“The clinical results presented today further support translation of our preclinical data to patients with severe asthma and suggest that the high potency of verekitug could lead to a potentially differentiated treatment profile with respect to both dosing interval and efficacy,” said Rand Sutherland, M.D., Upstream Bio’s Chief Executive Officer. “We continue to advance our two Phase 2 trials of verekitug in severe asthma and in chronic rhinosinusitis with nasal polyps, with the goal of observing continued durable effect with extended dosing intervals, a treatment paradigm that has the potential to advance care for patients with these diseases.”

The MAD study was a multicenter, randomized, double-blind, placebo-controlled trial that enrolled adults with mild to moderate asthma and elevated blood eosinophils. Four dosing cohorts were included: 100 mg every 4 weeks, 200 mg every 4 weeks, 300 mg every 12 weeks and 25 mg single dose. Participants were observed for 32 weeks following randomization (NCT05448651).

A digital version of the poster can be found on Upstream's website.

**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 Verekitug**

Verekitug is a novel recombinant fully human immunoglobulin G1 (IgG1) monoclonal antibody (mAb) that binds to the TSLPR and inhibits proinflammatory signaling initiated by TSLP. Verekitug is currently being evaluated in two Phase 2 clinical trials, the VALIANT trial in patients with severe asthma (NCT06196879) and the VIBRANT trial in patients with chronic rhinosinusitis with nasal polyps (CRSwNP) (NCT06164704). In preclinical studies, verekitug demonstrated high occupancy of the TSLPR 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 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, showed a predictable and consistent pharmacokinetic profile, and had high subcutaneous bioavailability.

**About Upstream Bio**

The focus of Upstream Bio is to maximize the potential of verekitug as a potential first-in-class antagonist of the TSLP receptor that may deliver best-in-class efficacy for people with severe asthma, CRSwNP, and other related diseases. Beyond these initial indications, Upstream Bio believes verekitug has broad potential in other inflammatory diseases, and it intends to leverage verekitug's differentiated attributes to develop it as a potential therapy for diseases where TSLP signaling has been shown to play a significant role.

**Company Contact**
Michael Gray
Chief Financial Officer and Chief Operating Officer
info@upstreambio.com

**Media Contact:**
Teri Dahlman
Red House Communications
teri@redhousecomms.com

---