



Upstream Bio Announces Oral Presentation of New Data from a Phase 1b Multiple Ascending Dose Trial of Verekitug (UPB-101) in Adults with Asthma at the European Respiratory Society Congress

September 9, 2024

– Treatment with verekitug led to rapid PD effects which were sustained for up to 24 weeks, supporting evaluation of dosing intervals of once every 12 or 24 weeks in ongoing Phase 2 clinical trials –

– PK/PD modeling predicts substantially higher clinical potency of verekitug compared to reported tezepelumab data –

WALTHAM, Mass. – September 9, 2024 – Upstream Bio, Inc., a clinical-stage company developing verekitug, an investigational antagonist of the Thymic Stromal Lymphopoietin (TSLP) receptor, today presents additional clinical data from its 32-week, Phase 1b multiple ascending dose trial of verekitug (UPB-101) in adults with asthma at the European Respiratory Society (ERS) Congress 2024 being held in Vienna, Austria.

New data from pooled verekitug-treated asthma patient cohorts demonstrated substantial reductions in biomarkers of inflammation including IL-5 (Interleukin 5) and IgE (immunoglobulin E), in line with previously reported effects on blood eosinophils and fractional exhaled nitric oxide (FeNO). Predictive modeling based on observed pharmacodynamic (PD) and pharmacokinetic (PK) parameters suggests that verekitug may exhibit high potency in asthma patients, with an approximately 1.5-fold greater maximal predicted reduction of FeNO compared to that reported for tezepelumab. PK/PD modeling predicts that verekitug 100 mg once every 12 weeks (Q12W) and 400 mg once every 24 weeks (Q24W) dosing regimens could maintain trough serum levels above FeNO EC90 levels for >95% of the dosing interval, supporting testing of these dosing regimens in the ongoing Phase 2 VALIANT clinical trial for verekitug in severe asthma.

As previously reported, verekitug was well tolerated at all dose levels tested. Verekitug also demonstrated rapid and substantial treatment effects, including 100% TSLP receptor occupancy after one dose, up to 54% reduction in FeNO and up to 65% reduction in blood eosinophils at 12 weeks. These findings were sustained for up to 24 weeks after the last dose.

“We are pleased to share data supporting the potential for a differentiated product profile for verekitug, the only known antagonist in clinical development targeting the TSLP receptor,” said Aaron Deykin, M.D., Upstream Bio’s Chief Medical Officer and Head of R&D. “TSLP receptor inhibition with verekitug has led to rapid, substantial

and sustained reductions in disease-related biomarkers that are known to predict a reduction in exacerbations, which are clinically meaningful to patients with asthma. The data and related PK/PD modeling suggest significant potency and support our evaluation of dosing intervals of every 12 or 24 weeks in our ongoing Phase 2 VALIANT clinical trial in severe asthma. We look forward to further understanding the potential of verekitug to improve clinical outcomes and enhance patient care.”

Oral data presentation details are as follows:

Date and Time: September 9, 2024, 2:50 p.m. CEST

Presentation Title: 32-week data from a multiple ascending dose trial with verekitug, a novel antibody to the human TSLP receptor (TSLPR), in adults with asthma

Session Title: Recent advances in biological treatments for asthma and chronic obstructive pulmonary disease

A digital version of the presentation can be found on Upstream’s [website](#).

About the Phase 1b MAD Study

The multiple ascending dose (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).

About TSLP and TSLP Receptor 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 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 potently binds to the TSLP receptor and inhibits proinflammatory signaling initiated by TSLP. Verekitug is the only known antagonist in clinical development targeting the TSLP receptor.

Three Phase 1 clinical trials have been completed for verekitug across a total of 120

participants, including 32 patients with asthma. In the Phase 1 single ascending dose (SAD) and Phase 1b multiple ascending dose (MAD) clinical trials, verekitug was well tolerated, demonstrated no evidence of clinically meaningful immunogenicity, showed a predictable and consistent pharmacokinetic profile, and had high subcutaneous bioavailability. Results of the Phase 1b MAD trial also demonstrated that verekitug is a potent inhibitor of the TSLP receptor and has the potential for an extending dosing interval compared to currently available treatments.

Verekitug is currently being evaluated in two placebo-controlled, multi-national, randomized Phase 2 clinical trials. The VALIANT trial is a Phase 2 clinical trial in an estimated 436 patients with severe asthma, in which verekitug is administered at dosing intervals of either once every 12 weeks or once every 24 weeks with a primary endpoint of annualized asthma exacerbation rate (NCT06196879). The VIBRANT trial is a Phase 2 clinical trial in approximately 70 patients with chronic rhinosinusitis with nasal polyps (CRSwNP), in which verekitug is administered at a dosing interval of once every 12 weeks with a primary endpoint of change from baseline in nasal polyp score at week 24 (NCT06164704).

About Upstream Bio

Upstream Bio is a clinical-stage biotechnology company developing treatments for inflammatory diseases, with an initial focus on severe respiratory disorders. Upstream Bio is developing verekitug, the only known antagonist currently in clinical development that targets the receptor for Thymic Stromal Lymphopoietin (TSLP). The focus of Upstream Bio is to maximize verekitug's unique attributes to address the substantial unmet needs of patients with severe asthma and CRSwNP that are underserved by today's standard of care. 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.

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