Upstream Bio Initiates a Phase 2 Clinical Trial of Verekitug (UPB-101) in Severe Asthma and Doses First Patients

Upstream announces the first global Phase 2 asthma study of a biologic inhibiting TSLP signaling including a 24-week dosing regimen and the potential to achieve best-in-class efficacy based on highly differentiated potency in asthma patients.

WALTHAM, Mass. – March 7, 2024 - Upstream Bio, a clinical-stage biotech company advancing new therapies to treat inflammation, today announced the dosing of the first patients in its Phase 2 VALIANT clinical trial of verekitug (UPB-101) in patients with severe asthma. Verekitug is a recombinant fully human immunoglobulin G1 monoclonal antibody designed to block the thymic stromal lymphopoietin receptor (TLSPR) and thus inhibit TSLP-driven inflammation. Verekitug is currently under investigation in a Phase 2 study for patients with chronic rhinosinusitis with nasal polyps (CRSwNP).

"We are thrilled to initiate the Phase 2 study in severe asthma after the findings from our multiple ascending dose (MAD) study in asthma patients demonstrated that verekitug produces a compelling reduction in disease-related biomarkers," said Aaron Deykin, Head of R&D and Chief Medical Officer. "The 100 mg dose in the MAD study showed a 54% reduction from baseline in FeNo and EOS at week 12 that was sustained through week 32, which was 24 weeks after the last dose. These observations not only demonstrate the higher potency of verekitug compared to published data from tezepelumab, but also enable Upstream to study extended dosing regimens in Phase 2 including every 24 weeks."

The VALIANT study is a randomized, double-blind, placebo-controlled study evaluating verekitug in doses of 100 mg every 24 weeks (Q24W), 400 mg Q24W, 100 mg every 12 weeks (Q12W), or placebo administered subcutaneously in a single injection. The study will evaluate verekitug's efficacy in the treatment of severe asthma as reflected by the registrational primary endpoint of the annual asthma exacerbation rate (AAER).

"Verekitug has the potential to be a best-in-class inhibitor of TSLP signaling based on its swift, substantial and sustained effect on clinically relevant biomarkers that are known to correlate with impact on AAER," said Sam Truex, Chief Executive Officer. "Our team is thrilled to carry our momentum from Phase 1b into our global Phase 2 studies where we intend to demonstrate how verekitug's high potency translates to clinical outcomes that will benefit patients with many types of asthma."

About Verekitug (UPB-101)

Verekitug is a novel recombinant fully human immunoglobulin G1 (IgG1) monoclonal antibody (mAb) that binds to the human thymic stromal lymphopoietin (TSLP) receptor (TSLPR) to inhibit signaling. In preclinical studies, verekitug demonstrated inhibition of cytokine production from both CD4+ T cells and ILC2, suggesting that it may be effective against multiple types of inflammation. Data in three Phase 1 studies conducted to date demonstrate that verekitug is safe and well-tolerated.

In a Phase 1b study, verekitug became the first TSLP signaling inhibitor to demonstrate sustained target engagement and maintain maximal inhibition of disease-related biomarkers in patients with asthma 24-weeks after the last study dose. Results of the Phase 1b study demonstrated that verekitug is a potent

inhibitor of TSLP-driven biology. It is the most advanced TSLP signaling inhibitor in global development and is the only agent with clinical data out to 32 weeks from a completed study in asthmatic patients.

The company's lead indication is asthma, a chronic disease of the lungs that affects approximately 350 million people worldwide and is often underdiagnosed and under-treated.[1] Of the more than 25 million people in the U.S. living with asthma[2], about 5-10% suffer from severe asthma. CRSwNP is a chronic disease of the upper airway that obstructs the sinuses and nasal passages. CRSwNP is highly comorbid with asthma, in fact up to 65% of patients with CRSwNP suffer from asthma.[3]

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 signaling is one of the first events in the inflammatory cascade stimulated by allergens, viruses, and other triggers. TSLP signaling activates downstream targets such as IL-4, IL-5, IL-13, IL-17 and IgE. Because TSLP is a target upstream in the inflammatory cascade, there is an opportunity to address disease at its root, prior to the influence of other disease-related cytokines. Inhibiting TSLP signaling by 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 Upstream Bio

At Upstream Bio we strive to reach the source of inflammation and conquer it. Our lead program, verekitug (UPB101), is a clinical-stage monoclonal antibody that inhibits the TSLP receptor. TSLP is a validated target positioned upstream of multiple signaling cascades that affect a variety of immune cells pivotal to common and rare diseases. We have completed Phase 1b in asthma and have initiated Phase 2 studies in both CRSwNP (Chronic rhinosinusitis with nasal polyps) and asthma in Q1 2024. We are leveraging our diverse roots and the team's substantial industry experience to develop verekitug to ease the burden of inflammatory and allergic diseases on patients and their loved ones.

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[1] EEACI Global Atlas of Asthma, April 2021

[2] American Lung Association, website, 2023

[3] Bachert C, Bhattacharyya N, Desrosiers M, Khan AH. Burden of Disease in Chronic Rhinosinusitis with Nasal Polyps. J Asthma Allergy. 2021 Feb 11;14:127-134. doi: 10.2147/JAA.S290424. PMID: 33603409; PMCID: PMC7886239