Upstream Bio Announces Dosing of First Patients in a Phase 2 Clinical Trial of Verekitug (UPB-101) in Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

CRSwNP Phase 2 program is the first multi-national Phase 2 trial with a TSLP pathway inhibitor to explore every-12-week dosing.

WALTHAM, Mass. – January 3, 2024 - Upstream Bio, a clinical-stage biotech company advancing new therapies to treat inflammation, today announced the dosing of the first patients in a Phase 2 clinical trial of verekitug in patients with chronic rhinosinusitis with nasal polyps (CRSwNP). 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. TSLP is a cytokine and a key driver of inflammatory response in CRSwNP, asthma, and other allergic and inflammatory diseases.

“Enabled by the large and durable effects of verekitug on exhaled nitric oxide and blood eosinophils demonstrated in our recently completed Phase 1b study in asthma patients, we are thrilled to now move verekitug into Phase 2 in CRSwNP. The high potency data documented in our previous studies support a dosing interval of at least every 12 weeks,” said Aaron Deykin, MD, Chief Medical Officer and Head of Research and Development. “We also plan to initiate a Phase 2 study in asthma this quarter that will include dosing intervals of 12 weeks and 24 weeks.”

The CRSwNP Phase 2 study is a randomized, double-blind, placebo-controlled study evaluating a dose of 100 mg administered subcutaneously in a single injection every 12 weeks. The study will evaluate verekitug’s efficacy in the treatment of CRSwNP with a primary endpoint of reduction in nasal polyp score. Data from the combination of Upstream Bio’s Phase 2 studies in CRSwNP and asthma will inform the dose regimen for Phase 3 in both indications.

“This Phase 2 trial presents the opportunity for Upstream Bio to demonstrate verekitug’s potential as a best-in-class biologic for the treatment of a broad range of allergic and inflammatory conditions,” said Sam Truex, Chief Executive Officer. “We expect that the swift, substantial and sustained reduction in disease-related biomarkers seen in the Phase 1b will translate to meaningful results for patients with CRSwNP in our Phase 2 study with the benefit of one injection and a 12-week dosing interval.”

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 opportunity to address disease at its root, prior to the influence of other disease-related cytokines. 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 (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

pre-clinical 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 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 inhibitor in development and is the only agent with clinical data out to 32-weeks in asthmatic patients. The Phase 1b study in asthma demonstrated a swift, substantial and sustained effect on FeNO and blood eosinophils which potentially represents best in class potency and inhibition of disease-related biomarkers.

The company's lead indication is asthma, a chronic disease of the lungs that affects approximately 350 million people worldwide and is often under-diagnosed 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 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 are opening 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.