Upstream Bio Announces Positive Phase 1b Interim Data in Asthma and Company Progress Toward Phase 2

UPB-101 safety, tolerability, and PK/PD results support advancing to Phase 2 in Q1 2024

Findings reveal potency and receptor occupancy supporting Phase 2 dosing regimens at 12-week and 24-week intervals

WALTHAM, Mass. – October 24, 2023 - Upstream Bio, a clinical-stage biotech company advancing new therapies to treat inflammation, today announced positive interim results in its Phase 1b clinical study of UPB-101, a thymic stromal lymphopoietin receptor (TSLPR) inhibitor. The Phase 1b study is a randomized, double-blinded, placebo-controlled multiple ascending dose (MAD) study with subcutaneous (SC) administration conducted in asthma patients. The interim data results demonstrated favorable safety, tolerability, immunogenicity, pharmacokinetic (PK) and pharmacodynamic (PD) markers that strongly support moving to Phase 2.

The Phase 1b trial enrolled 32 asthmatic subjects at 4 sites in the UK into four cohorts of doses: 100 mg every 4 weeks, 200 mg every 4 weeks, 300 mg every 12 weeks and a single dose of 25 mg. Within each cohort, subjects were randomized 6:2 to UPB-101 or placebo. At the week 24 interim evaluation, UPB-101 was safe and well tolerated and demonstrated full receptor saturation in all doses studied. Furthermore, UPB-101 was demonstrated to be a potent suppressor of the disease-related biomarker, fractional exhaled nitric oxide (FeNO). PK/PD modelling indicated a maximal FeNO reduction from baseline (Emax) of 43%. PK observations support exploration of extended interval dose regimens in Phase 2.

Detailed topline results are expected to be presented at an upcoming congress.

“These results confirm the high potency of UPB-101 and thus indicate that 12- and 24-week extended interval dosing is appropriate. In this regard, we are excited to pursue both 12- and 24-week regimens in our Phase 2 trial in severe asthma,” said Aaron Deykin, MD, Chief Medical Officer and Head of Research and Development.

Additionally, the company has completed a randomized, double-blinded, placebo-controlled Phase 1 single dose study of UPB-101 in 32 participants representing Japanese and non-east Asian healthy volunteers. The study demonstrated PK/PD and safety data entirely consistent with existing data previously generated in Western populations studied in other trials. This study included doses of 100 mg, 200 mg and 300 mg.

In June of this year, the company raised a Series B private capital round to pursue registrational Phase 2 clinical trials in asthma and chronic rhinosinusitis with nasal polyps (CRSwNP). The company has also grown to 30 people who are highly experienced biotech professionals managing multiple mid-stage clinical trials in partnership with an established global CRO partner.

“As expected, the Phase 1b study supports continued exploration of the safety and efficacy of UPB-101 at dose intervals that may provide patients and their caregivers with options to extend their dose to every 12 weeks or even every 24 weeks,” added Samantha Truex, CEO. “The Upstream team is taking swift steps to move into our global Phase 2 studies in severe asthma and CRSwNP by Q1 2024. These

data indicate that UPB-101 and TSLPR inhibition have the potential to offer best-in-class advantages that have yet to be realized across current treatment options."

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 Phase 1b Trial in Asthma (NCT 05448651) and Phase 1 Japanese healthy volunteer Trial (NCT 05653479)

The Safety and Biologic Impact (Pharmacodynamics) of Repeated Injections and Increasing Amounts of UPB-101 in Asthmatics (Phase 1b study in Asthma) is a randomized, double-blinded, placebo-controlled multiple ascending dose (MAD) study with subcutaneous (SC) administration conducted in asthma patients. It was designed to demonstrate clinical evidence of safety, tolerability, pharmacokinetic (PK), pharmacodynamic (PD) and immunogenicity. The Phase 1 single dose study in Japanese and non-east Asian healthy volunteers is a randomized, double-blinded, placebo-controlled Phase 1 single dose study of UPB-101. It was designed to demonstrate clinical evidence of safety, tolerability, pharmacokinetic (PK), pharmacodynamic (PD) and immunogenicity.

About UPB-101

UPB-101 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. UPB-101 is designed to address allergic and inflammatory diseases including asthma. In pre-clinical studies, UPB-101 demonstrated inhibition of cytokine production from both CD4+ T cells and ILC2, and completely suppressed skin allergic reactions in a monkey model, suggesting that it may be effective against multiple types of inflammation. Data in all three Phase 1 studies conducted to date demonstrate that UPB-101 is safe and well-tolerated.

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, UPB-101, 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 are leveraging our diverse roots and the team's substantial industry experience to develop therapies that ease the burden of inflammatory and allergic diseases on patients.

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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.