Upstream Bio Announces Dosing of First Patient in a Phase 1b Clinical Trial of UPB-101 in Asthma

UPB-101 is a thymic stromal lymphopoietin receptor (TLSPR) blocker that inhibits signaling at the top of the inflammatory cascade

WALTHAM, Mass. – August 9, 2022 - Upstream Bio, a clinical-stage biotech company advancing new therapies to treat inflammation, today announced the initiation of a Phase 1b multiple ascending dose study of UPB-101 in asthma patients and successful dosing of the first patient. UPB-101 is a 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 asthma and other allergic and inflammatory diseases.

"The Upstream team is excited to bring UPB-101 to asthma study participants. Our goals with this study are to further explore the impact of UPB-101 on relevant pharmacodynamic measures, and to inform the dose regimen selection for Phase 2 investigation," said Aaron Deykin, MD, Chief Medical Officer and Head of Research and Development. "TSLP receptor blockade is a novel approach to inhibiting TSLP-induced activation of multiple downstream pathways in asthma and is anticipated to have broad utility across many inflammatory phenotypes of patients. It is an emerging class of biologics for patients with moderate to severe asthma who, despite treatment with standard inhaled medications, still experience ongoing exacerbations and debilitating, sometimes life-threatening symptoms."

The Phase 1b study is a randomized, double-blind, placebo-controlled, multiple ascending dose study. The completion of the study is expected in 2023. The study is designed to further characterize UPB-101 based on a previous Phase 1 single ascending dose study of healthy volunteers completed by Astellas Pharma. In the single ascending dose study, UPB-101 demonstrated a promising profile on safety, pharmacokinetics, and pharmacodynamics measures. 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 non-human primate model, suggesting that it may be effective against multiple types of inflammation.

"Advancing UPB-101 to a multiple ascending dose trial in asthma patients marks a key milestone for our team. We anticipate that UPB-101's unique mechanism targeting the TSLP receptor upstream of the inflammatory cascade has the potential to benefit patients living with uncontrolled asthma and other inflammatory indications," said Sam Truex, Chief Executive Officer.

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 TSLP expression is elevated across lung tissues and blood compared with healthy individuals and correlates with airway obstruction and disease severity. In addition, Genome-Wide Association Studies have identified associations between asthma risk and polymorphisms in the TSLP gene.

TSLP activation is one of the first events in the inflammatory cascade stimulated by allergens, viruses, and other triggers, initiating the upregulation 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, 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 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 and their loved ones. https://www.upstreambio.com/

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