Upstream Bio Announces the Appointment of Marcella Ruddy, M.D., to the Board of Directors

WALTHAM, Mass. –February 7, 2022 - <u>Upstream Bio</u>, a clinical-stage biotech company advancing new therapies to treat inflammation, today announced the appointment of Dr. Marcella Ruddy to its Board of Directors. Dr. Ruddy is the Chief Medical Officer of Tectonic Therapeutic. Dr. Ruddy has an extensive background in drug development and inflammation from her work as both a clinician and the previous Head of Clinical Development for the Immunology/Inflammation therapeutic area at Regeneron Pharmaceuticals, where she was instrumental in driving development of dupilumab across multiple indications.

Dr. Ruddy will transition from her previous role as a clinical advisor to Upstream to a Board member, continuing to provide valuable strategic input regarding the development of 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 currently in a Phase 1b multiple ascending dose study in asthma patients.

"It is a pleasure to welcome Marcie, a highly experienced industry leader, to our Board of Directors," said Sam Truex, Chief Executive Officer of Upstream Bio. "Her deep drug development and clinical expertise in asthma and other inflammation-driven diseases are invaluable as we advance our program and plan expansion into new indications to address unmet needs for patients. Marcie's background is an important addition to our board and a key step toward diversifying the perspectives represented in our Board discussions."

"I am delighted to join the Board at this exciting time in the Company's evolution," said Dr. Ruddy, "The accomplishments of the team to date have been noteworthy and I'm looking forward to continuing to be part of the progress at Upstream Bio. The company is well positioned to execute on its mission to stop inflammation at its source via TSLP receptor inhibition."

Dr. Ruddy has over 18 years of drug development experience. Before Regeneron, Dr. Ruddy held clinical leadership positions at Alnylam, EMD Serono and Merck Research labs where she oversaw the early clinical development of programs across multiple therapeutic areas including inflammation, respiratory, muscle, metabolic and rare diseases. She is a board-certified pulmonologist and held a staff position in the Pulmonary Unit at Massachusetts General Hospital/Harvard Medical School where she founded and directed the Adult Cystic Fibrosis Program. Earlier in her career, she completed her Internal Medicine Residency and Pulmonary Critical Care Fellowship training at Harvard Medical School and associated medical centers. Dr. Ruddy holds an AB (Bachelor of Arts) from Princeton University and a Doctor of Medicine from Washington University, St Louis.

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 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.

Dosing in the first-in-human Phase 1, randomized, placebo-controlled, single dose-escalation study in healthy volunteers was considered safe and well-tolerated. A follow-on Phase 1b multiple ascending dose study in people diagnosed with asthma is underway.

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. <u>https://www.upstreambio.com/</u>

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