Tectonic Therapeutic Initiates Phase 1B Study for TX45 in Group 2 Pulmonary Hypertension in Patients with Preserved Ejection Fraction Heart Failure

Study to evaluate TX45 impact on cardiopulmonary hemodynamics in patients with Group 2 Pulmonary Hypertension, a patient population in urgent need of novel therapies

TX45 clinical program advancing on track based on promising initial Phase 1A data; confirmatory Phase 1A data expected mid-2024 and topline Phase 1B data expected in 2025

Watertown, MA (March 26, 2024) – Tectonic Therapeutic, Inc. ("Tectonic"), a privately-held biotechnology company developing GPCR (G-protein coupled receptor)-targeted therapeutic proteins, co-founded by Timothy A. Springer and Andrew C. Kruse of Harvard Medical School, today announced the initiation of enrollment in the Phase 1B study for TX45, an investigational long-acting relaxin-Fc fusion molecule. The study will evaluate the safety and hemodynamic effects of single-dose TX45 in patients with Group 2 Pulmonary Hypertension secondary to Heart Failure with preserved Ejection Fraction (Group 2 PH with HFpEF).

Group 2 PH with HFpEF impacts over 600,000 patients in the US and is associated with significant morbidity and mortality. Importantly, there are no approved therapies for this condition. "Our goal is to leverage relaxin's vasodilatory, anti-fibrotic and anti-inflammatory properties to provide improved treatment outcomes for patients with Group 2 PH," said Alise Reicin, MD, President and CEO at Tectonic. "It has long been hypothesized that the unique biology of relaxin may offer substantial therapeutic potential in the treatment of cardiovascular disease. This study will provide us with valuable TX45 pharmacology and hemodynamic data in patients."

Demonstrating a durable treatment effect with the native relaxin protein can be challenging due to its intrinsic short half-life; however, initial data from Tectonic's ongoing Phase 1A study suggests that TX45 has the potential to overcome previous challenges and to be a best-in-class therapy. Topline results from the Phase 1A study are expected to be reported in mid-2024, followed by results from the Phase 1B study in Group 2 PH with HFpEF patients in 2025. A randomized Phase 2 study is planned to begin in H2 2024.

Phase 1B study overview

The Phase 1B study with TX45 in patients with Group 2 PH with HFpEF is a single dose, open-label study to evaluate safety, tolerability and acute hemodynamic effects of intravenous administration of TX45. The study will evaluate the effect of TX45 on hemodynamic parameters, as determined by right heart catheterization and echocardiography.

About TX45, a long-acting Fc-relaxin fusion protein

Known as a "pregnancy hormone," relaxin is upregulated during pregnancy to help the expectant mother's cardiovascular system meet the increased demand from the developing fetus, and to remodel tissues and musculoskeletal structures involved in childbirth. Because of these features, it offers a

similarly broad range of potential therapeutic applications with significant benefits expected in cardio-pulmonary diseases.

Tectonic's TX45 Fc-relaxin fusion protein is a potential best-in-class agent, resulting from protein engineering efforts to overcome limitations associated with the natural human hormone and achieve both optimal *in vitro* (biophysical and developability), as well as *in vivo* (pharmacokinetic and pharmacodynamic, or "PK/PD") properties. Tectonic is leveraging relaxin's vasodilatory and anti-fibrotic properties with the goal of improving treatment outcomes for patients with Group 2 PH.

About Pulmonary Hypertension and HFpEF

The World Health Organization has defined 5 groups of pulmonary hypertension (PH). Tectonic is focused on the Group 2 subtype, a condition that develops as a consequence of left-sided heart disease, specifically pulmonary hypertension secondary to left heart failure with preserved ejection fraction (PH-HFpEF). There are an estimated 6 million patients with heart failure in the United States, with HFpEF representing up to ~50% of heart failure cases. Tectonic estimates the combined Group 2 PH population with HFpEF at over 600,000. In this condition, chronic heart failure leads to increased blood pressure in the pulmonary arteries, exerting severe strain on the right side of the heart, which adapts poorly to the increased pressure. This increased pulmonary pressure gradually causes worsening exercise capacity, shortness of breath and right-sided heart failure which can lead to death. Although several Group 1 PH (PAH) medications have been explored in Group 2 PH, no medications have yet demonstrated consistent efficacy, and to date, none have been approved for its treatment.

About Tectonic Therapeutic

Tectonic Therapeutic, co-founded by Andrew Kruse and Tim Springer of Harvard Medical School, is transforming the discovery of antibodies and other biologic drugs targeting GPCRs to develop novel therapies for patients inadequately served by current treatments. With its proprietary GEODe™ platform, Tectonic aims to unlock the therapeutic utility of some of the most difficult receptors in the class, where small molecule pharmacology may be intractable. In January 2024, Tectonic entered into a definitive agreement to merge with AVROBIO, Inc. (Nasdaq: AVRO). Tectonic is headquartered in Watertown, Massachusetts. Learn more at www.tectonictx.com and follow us @TectonicTx.

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