First Participant Dosed in Tisento Therapeutics' Global Phase 2b PRIZM Study Evaluating Zagociguat for the Treatment of MELAS

Patient-Centered PRIZM Study Measures Impact of Once-Daily Oral Zagociguat on Fatigue and Cognitive Impairment, Hallmark Features of this Rare Mitochondrial Disease

CAMBRIDGE, Mass., January 27, 2025 – Tisento Therapeutics today announced that the first patient has been dosed in its global Phase 2b PRIZM study. The study is investigating the impact of once-daily oral zagociguat treatment on fatigue, cognitive impairment, and other key aspects of the rare mitochondrial disease MELAS (Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like Episodes).

The PRIZM study is centered in multiple ways on what matters to people living with MELAS. The study incorporates features that maximize convenience for participants, including at-home assessments, the potential for at-home study visits, and door-to-door travel support. In addition, all participants will receive zagociguat during one period of this crossover study, and participants who complete the study may be eligible for continued access via an open-label extension study. Importantly, the clinical outcome assessments and endpoint strategy for the PRIZM study were informed by Tisento's interview study in which individuals living with MELAS described the symptoms and impacts of the disease that are most important to them. PRIZM is a global study now enrolling in North America, Europe, and Australia. Patients and families interested in learning more can visit Tisento's PRIZM page, ClinicalTrials.gov (NCT06402123), or discuss with their physician.

"Since Tisento's founding, we have been focused on initiating a thoughtful, well-designed clinical study to evaluate zagociguat for the treatment of MELAS, and we are humbled by the enthusiastic response we have received from physicians and the mitochondrial disease community," said Peter Hecht, PhD, chief executive officer of Tisento. "We are pleased that the first participants are enrolling in the global PRIZM study, which was designed with patient perspectives at the forefront. We will continue to put patients first every step of the way as we work to develop creative solutions to address what matters most for people with serious diseases."

"MELAS is the most common condition we see in our mitochondrial clinic, with profound effects on patients' daily lives and wellbeing. Right now, we have no approved treatments, making the search for effective therapies absolutely critical," said Dr. Austin Larson, associate professor of pediatric clinical genetics and metabolism at the University of Colorado School of Medicine and PRIZM study investigator. "I am excited about zagociguat's potential to address both the severe fatigue and cognitive challenges that so significantly impact our MELAS patients."

About the PRIZM Study

PRIZM – a **P**hase 2b **R**andomized, Placebo-Controlled Trial **I**nvestigating **Z**agociguat in **M**ELAS – is evaluating the efficacy and safety of oral zagociguat 15 mg or 30 mg compared to placebo when administered once-daily for 12 weeks in participants with genetically and phenotypically defined MELAS. The PRIZM study has a crossover design, with two 12-week treatment periods separated by a 4-week washout period. All participants will receive zagociguat during one of the 12-week periods and placebo during the other. Participants who complete the study may be eligible for an open-label extension study.

PRIZM is a global study that will enroll approximately 44 participants at mitochondrial disease centers of excellence in the U.S., Italy, Germany, United Kingdom, Australia, and Canada. For more information, please visit www.tisentotx.com/prizm or ClinicalTrials.gov (NCT06402123) for more information. Interested individuals can also reach out to their physicians for participation details.

About Zagociguat

Zagociguat is a once-daily, oral, clinical-stage investigational medicine with potential to positively impact both peripheral and central nervous system manifestations of mitochondrial diseases. Zagociguat stimulates soluble guanylate cyclase (sGC), an enzyme that is found in virtually every cell in every tissue of the body and is part of a system of cellular mechanisms that control critical physiological functions including neuronal function and blood flow.

A first-in-class, brain-penetrant sGC stimulator, zagociguat is hypothesized to rebalance dysregulated cellular pathways in MELAS. By restoring cellular functions that support mitochondria, zagociguat may help restore mitochondrial energy production and physiological function.

In a Phase 2a study in patients with MELAS, zagociguat exhibited a favorable safety profile, exposure throughout the body including in the central nervous system, and improvements in neuronal function, mitochondrial function, and blood flow in the brain. Zagociguat is currently being evaluated as a treatment for MELAS in the Phase 2b PRIZM study.

For more information, visit www.tisentotx.com/our-science.

About Tisento Therapeutics

Tisento Therapeutics, a privately held biotech company, is developing novel medicines to treat diseases with significant unmet need, beginning with MELAS and other genetic mitochondrial diseases. *Ti sento* means “I hear you” in Italian; our approach to innovation begins with listening to patients and then channeling what we learn into decisive actions that shape our research and clinical programs.

Tisento is guided by a high-caliber internal team of biopharma veterans and an extensive external network of expert physicians, patient advocacy groups, researchers, industry-leading vendors, and other close collaborators who are partners in our mission to develop meaningful treatments for mitochondrial diseases.

Learn more at our website, www.tisentotx.com, or connect with us on LinkedIn (Tisento Therapeutics) or X (@tisentotx).

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