Graybug Vision Concludes Patient Enrollment in its Phase 2b Clinical Trial of GB-102 in Wet Age-Related Macular Degeneration and Accelerates Trial Read-out by Approximately Six Months

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REDWOOD CITY, Calif., March 18, 2020 (GLOBE NEWSWIRE) -- Graybug Vision, Inc., a clinical stage biopharmaceutical company focused on developing transformative medicines to treat diseases of the retina and optic nerve, today announced the early closing of enrollment in its ALTISSIMO trial. ALTISSIMO is a Phase 2b, 12-month, multicenter, prospective, masked, randomized trial that compares each of two dosing regimens of GB-102 (1 or 2 mg), administered every six months, to aflibercept, administered every two months, in patients with anti-vascular endothelial growth factor (anti-VEGF)-responsive wet age-related macular degeneration (wet AMD). Since launching ALTISSIMO in September 2019, 56 patients have been enrolled at 33 clinical sites in the United States. A limited interim safety analysis performed in February 2020 supports Graybug's intention to take the 1 mg dose forward for further exploration in clinical trials, ultimately resulting in the acceleration of the ALTISSIMO final data analysis by approximately six months.

"GB-102 has the potential to help patients control their disease by addressing the treatment burden of wet AMD with a single injection every six months. Improving the safety of GB-102 by reducing the rate of anterior chamber migration of microparticles is important for both clinicians and patients. This has been a key focus in multiple ongoing trials and the data has now shown that the 1 mg dose of the newly optimized formulation is appropriate for use in the pivotal trials," said Arshad M. Khanani, M.D., M.A., Managing Partner and Director of Clinical Research, Sierra Eye Associates, and Clinical Associate Professor of Ophthalmology, University of Nevada.

Graybug's lead product candidate, GB-102, a microparticle depot formulation of the anti-VEGF sunitinib malate, seeks to reduce the need for frequent intravitreal (IVT) injections by expanding treatment duration to six months and reducing the burden of current treatments. Emerging evidence from Graybug's three dose-finding clinical trials suggests that 1 mg of GB-102 may offer improved safety and tolerability compared to the 2 mg dose of GB-102.

In Graybug's ADAGIO open-label Phase 1/2a clinical trial of 32 wet AMD patients that concluded in January 2019, GB-102 met its primary endpoint of safety and tolerability and provided evidence of durable biological activity for up to eight months from a single IVT injection in wet AMD patients. Particle migration in the anterior chamber was the most commonly reported drug-related adverse event in both the 1 mg and 2 mg doses. However, these events were generally self-limited, reversible, and without long-term sequalae. The manufacturing process of GB-102 was subsequently optimized, and preclinical testing showed enhanced aggregation properties.

In Graybug's ongoing, open-label Phase 2a clinical trial of GB-102 in 21 patients with macular edema secondary to diabetic macular edema and retinal vein occlusion initiated in September 2019, the safety and tolerability of a single dose of 1 mg or 2 mg GB-102 is being evaluated for six months. In January 2020, a three-month safety analysis of this open-label trial provided further evidence demonstrating the safety of the 1 mg dose, with a reduced number of particle migration events compared to the ADAGIO trial, while the rate of drug-related adverse events in the 2 mg arm remained unchanged. All patients will be monitored through the end of the trial at six months.

Subsequently, Graybug performed a limited safety analysis of the 56 patients enrolled in the ongoing ALTISSIMO trial. A pooled interim safety analysis of the ALTISSIMO and ME trials confirmed that the 1 mg dose exhibited less particle migration than the 2 mg dose. Consequently, the ALTISSIMO protocol has been amended to allow patients originally randomized to the 2 mg dose to perform their repeat dosing at six months with the 1 mg dose.

"We are confident that with over 40 patients receiving 1 mg of GB-102 through the 12-month endpoint, the ALTISSIMO trial will have a sufficiently large sample size to inform the design for our Phase 3 program of GB-102 in wet AMD, while preserving the trial's scientific integrity since the dosing regimen will remain masked. We expect the ALTISSIMO trial read-out to occur approximately six months earlier than originally planned," concluded Dr. Frederic Guerard, CEO of Graybug Vision.

About GB-102
GB-102 is a potent small molecule multiple receptor tyrosine kinase inhibitor, sunitinib malate, in a proprietary microparticle formulation designed to be administered intravitreally every six months. Sunitinib is gradually released from the microparticle formulation into the vitreous chamber and is designed to sustain therapeutic drug levels in the ocular tissues for up to six months.

About the Phase 1/2a ADAGIO Trial (wet AMD)
The ADAGIO clinical trial was an open-label, single dose trial of 32 patients from eight centers located in the United States, completed in January 2019. Patients enrolled in the trial were previously treated with at least three prior IVT injections of an anti-VEGF agent (aflibercept, bevacizumab or ranibizumab). They received a single intravitreal dose of GB-102 (0.25, 0.5, 1, or 2 mg) in escalating dose cohorts with eight patients in each cohort who were followed monthly for eight consecutive months. Depending on the dosage, between 50 and 88 percent of patients required no additional IVT injections of any anti-VEGF for six months after a single administration of GB-102.

About the Phase 2a Macular Edema Trial
The Phase 2a trial of GB-102 in patients with macular edema secondary of diabetic macular edema and retinal vein occlusion was initiated in September 2019 and enrolled 21 patients from six clinical sites in the United States. Eligible patients received a single IVT injection of either 1 or 2 mg GB-102 and are being followed for six consecutive months. The primary objective is to evaluate the safety, tolerability, and pharmacodynamic response of both doses. The trial is expected to conclude in the second quarter of 2020. For more information, please refer to: https://clinicaltrials.gov/ct2/show/NCT04085341.

About the Phase 2b ALTISSIMO Trial (wet AMD)
ALTISSIMO is a 12-month, multicenter, prospective, masked, randomized (3:3:2), 3-parallel arm design comparing two dosing regimens of GB-102 (1

or 2 mg) administered every six months to aflibercept administered every two months in patients with anti-VEGF-responsive wet AMD. The trial enrolled its first patient in September 2019, with an original enrollment goal of approximately 160 patients, at about 110 clinical sites in the United States. The protocol has been amended after an interim safety analysis to allow patients originally randomized to the 2 mg dose to perform their repeat dosing at six months with the 1 mg dose, and enrollment concluded after 56 patients were enrolled. The objective of the ALTISSIMO trial is to determine time-to-rescue and pharmacodynamic response to advance GB-102 to Phase 3 clinical trials in wet AMD. For more information, please refer to: https://clinicaltrials.gov/ct2/show/NCT03953079.

About Wet AMD

Wet AMD is one of the most common retinal diseases, leading to vision decline caused by excess VEGF. VEGF is a protein produced by cells that stimulates the formation of abnormal new blood vessels behind the retina, called choroidal neovascularization. The leakage of fluid and protein from the vessels causes retinal degeneration and leads to severe and rapid loss of vision. Early intervention is essential to treat wet AMD. According to the American Academy of Ophthalmology, the prevalence of wet AMD in the United States is estimated at 1.75 million people. We estimate that approximately 20 million adults are affected by wet AMD worldwide.

About Graybug Vision

Graybug Vision is a clinical stage biopharmaceutical company focused on developing transformative medicines to treat diseases of the retina and optic nerve. The company's proprietary ocular delivery technologies are designed to maintain effective drug levels in ocular tissue for up to six months and potentially longer, improving patient compliance, reducing healthcare burdens and ultimately delivering better clinical outcomes. Graybug's lead product candidate, GB-102, a microparticle depot formulation of sunitinib malate, inhibits multiple neovascular pathways for the intravitreal treatment of retinal diseases, including wet age-related macular degeneration, with a six-month dosing regimen. This approach is differentiated from the current standard of care, which requires more frequent dosing and primarily targets one neovascular pathway. Graybug is also using its proprietary technologies to develop GB-401, an injectable depot formulation of a beta-adrenergic prodrug, for primary open angle glaucoma, with a dosing regimen of up to six months, and GB-103, a longer-acting version of GB-102, designed to maintain therapeutic drug levels in the retinal tissue for 12 months with a single injection. Founded in 2011 as a spin-out of the Wilmer Eye Institute of the Johns Hopkins University School of Medicine, Graybug is headquartered in Redwood City, California. For more information, please visit www.graybug.com.

Media contacts

Bettina Maunz
404.384.0067
bmaunz@graybug.com

Lisa Lilienthal
404.661.3679
lisa@dialogue.marketing