Iveric Bio Announces FDA Has Granted Breakthrough Therapy Designation for Avacincaptad Pegol for Geographic Atrophy

November 17, 2022

- Designation based on 12-month primary endpoint data from GATHER pivotal trials -

- Avacincaptad pegol (ACP) is the only investigational product for treatment of GA to achieve two positive phase 3 pivotal trials with statistical significance -

- In GATHER clinical program, ACP achieved observed efficacy rates of up to 35% that increased over time -

PARSIPPANY, N.J.--(BUSINESS WIRE)--Nov. 17, 2022-- IVERIC bio, Inc. (Nasdaq: ISEE) today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation for avacincaptad pegol (ACP, also known as Zimura®), a novel investigational complement C5 inhibitor for the treatment of geographic atrophy (GA) secondary to Age-Related Macular Degeneration (AMD). To date, ACP is the first and only investigational therapy to receive Breakthrough Therapy designation status for this indication, which was granted based on the 12-month pre-specified primary endpoint data in the GATHER1 and GATHER2 pivotal clinical trials.

Breakthrough Therapy designation is designed to accelerate the development and regulatory review of potential new medicines that are intended to treat a serious condition and address a significant unmet medical need. The new medicine needs to show preliminary clinical evidence that the drug may demonstrate substantial improvement in effectiveness or safety over available therapies on a clinically significant endpoint and in general, should show a clear advantage.[1]

“We believe this Breakthrough designation reflects the fact that both GATHER1 and GATHER2 met their primary endpoint with a safety profile that meets the stringent criteria required,” said Glenn P. Sblendorio, Chief Executive Officer of Iveric Bio. “We are now focused on the execution of our full NDA submission and launch preparation, with the possibility of being first to market. We look forward to working collaboratively with the FDA to expedite the review timeline for avacincaptad pegol and to potentially bringing a new therapy to AMD patients impacted by GA.”

Recently, Iveric Bio announced the submission of the first part of its New Drug Application (NDA) for rolling review, which included the full clinical data package from the GATHER1 and GATHER2 pivotal trials. The company is on track to complete the final part of the NDA submission by the end of this year.

“In both GATHER1 and GATHER2, avacincaptad pegol consistently showed a treatment effect with the first measurement at month 6 that was persistent and continued to increase over time, with observed efficacy rates of up to 35%,” said Pravin U. Dugel, MD, President of Iveric Bio. “We believe ACP has the potential to safely and effectively preserve central vision by saving photoreceptor cells for patients living with this life-changing disease that leads to irreversible blindness.”

The FDA’s Breakthrough Therapy designation decision was based on the 12-month primary efficacy endpoint data from the GATHER1 and GATHER2 pivotal studies which evaluated the safety and efficacy of ACP in patients with GA located inside and/or outside of the clinical fovea. Per the special protocol assessment (SPA) agreement for GATHER2, the FDA required the mean rate of growth (slope) in GA area from baseline to month 12. These results showed a significant treatment difference of 35% (p=0.0050; GATHER1) and 18% (p= 0.0039, GATHER2) compared to sham using observed (non-transformed) data; and 28% (p=0.0063; GATHER1) and 14% (p= 0.0064; GATHER2) using square root transformation. In both GATHER1 and GATHER2 there were no events of serious intraocular inflammation, vasculitis, or endophthalmitis.

About Geographic Atrophy

Age-related macular degeneration (AMD) is the major cause of moderate and severe loss of central vision in aging adults, affecting both eyes in the majority of patients. The macula is a small area in the central portion of the retina responsible for central vision. As AMD progresses, the loss of retinal cells and the underlying blood vessels in the macula results in marked thinning and/or atrophy of retinal tissue. Geographic atrophy, the advanced stage of AMD, leads to further irreversible loss of vision in these patients. There are currently no U.S. FDA or European Medicines Agency (EMA) approved treatment options available for patients with geographic atrophy secondary to AMD.

About Avacincaptad Pegol

Avacincaptad pegol (ACP) is an investigational drug that has not yet been evaluated by any regulatory body for safety and efficacy. ACP is not authorized for any indication in any country. ACP is a novel complement C5 protein inhibitor. Overactivity of the complement system and the C5 protein are suspected to play a critical role in the development and growth of scarring and vision loss associated with geographic atrophy (GA) secondary to age-related macular degeneration (AMD). By targeting C5, ACP has the potential to decrease activity of the complement system that causes the degeneration of retinal cells and potentially slow the progression of GA.

About the GATHER Clinical Trials Supporting Breakthrough Therapy Designation

ACP met its primary endpoint in the ongoing randomized, double-masked, sham-controlled, multicenter GATHER1 and GATHER2 Phase 3 clinical trials. These clinical trials measured the efficacy and safety of monthly 2 mg intravitreal administration of ACP in patients with GA secondary to AMD. For the first 12 months in both trials, patients were randomized to receive either ACP 2 mg or sham monthly. There were 286 participants enrolled in

GATHER1 and 448 participants enrolled in GATHER2. The primary efficacy endpoints in both pivotal studies were based on GA area measured by fundus autofluorescence (FAF) at three time points: Baseline, Month 6, and Month 12. This primary endpoint is reflective of photoreceptor death and disease progression. In GATHER1 and GATHER2 combined, the most frequently reported treatment emergent adverse events in the 2 mg recommended dose were related to injection procedure. The most common adverse reactions (≥ 5% and greater than sham) reported in patients who received avacincaptad pegol 2 mg were conjunctival hemorrhage (13%), increased IOP (9%), and CNV (7%).

About Breakthrough Therapy Designation

Breakthrough therapy designation is intended to expedite the development and review of drugs for serious or life-threatening conditions. The criteria for breakthrough therapy designation require preliminary clinical evidence that demonstrates the drug may have substantial improvement on at least one clinically significant endpoint over available therapy. Approaches to demonstrating substantial improvement include the following:

- Direct comparison of the new drug to available therapy shows a much greater or more important response
- If there is no available therapy, the new drug shows a substantial and clinically meaningful effect on an important outcome when compared with a placebo or a well-documented historical control.
- The new drug added to available therapy results in a much greater or more important response compared to available therapy in a controlled study or to a well-documented historical control.
- The new drug has a substantial and clinically meaningful effect on the underlying cause of the disease, in contrast to available therapies that treat only symptoms of the disease, and preliminary clinical evidence indicates that the drug is likely to have a disease modifying effect in the long term (e.g., a sustained clinical benefit compared with a temporary clinical benefit provided by available therapies).
- The new drug reverses or inhibits disease progression, in contrast to available therapies that only provide symptomatic improvement.
- The new drug has an important safety advantage that relates to serious adverse reactions (e.g., those that may result in treatment interruption) compared with available therapies and has similar efficacy.

A breakthrough therapy designation conveys more intensive FDA guidance on an efficient drug development program, an organizational commitment involving senior managers, and eligibility for rolling review and priority review. FDA will review the full data submitted to support approval of drugs designated as breakthrough therapies to determine whether the drugs are safe and effective for their intended use before they are approved for marketing.

About Iveric Bio

Iveric Bio is a science-driven biopharmaceutical company focused on the discovery and development of novel treatments for retinal diseases with significant unmet medical needs. The Company is committed to having a positive impact on patients' lives by delivering high-quality, safe and effective treatments designed to address debilitating retinal diseases including earlier stages of age-related macular degeneration. For more information on the Company, please visit www.ivericbio.com.

Forward-looking Statements

Any statements in this press release about the Company's future expectations, plans and prospects constitute forward-looking statements for purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. Forward-looking statements include any statements about the Company's strategy, future operations and future expectations and plans and prospects for the Company, and any other statements containing the words "anticipate," "believe," "estimate," "expect," "intend", "goal," "may", "might," "plan," "predict," "project," "seek," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions. In this press release, the Company's forward-looking statements include statements about its expectations regarding the results and implications of the clinical data from its GATHER1 and GATHER2 trial of ACP in geographic atrophy, its development and regulatory strategy for ACP, including its plans to complete its submission of a new drug application to the U.S. Food and Drug Administration, the impact of FDA designations and the potential approvability and timelines for review of ACP, and the potential utility of ACP in treating geographic atrophy. Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's development programs, future results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, those related to expectations for regulatory matters, interpretation of clinical trial results by the scientific and medical community, developments from the Company's competitors and the marketplace for the Company's products, and other factors discussed in the "Risk Factors" section contained in the quarterly and annual reports that the Company files with the Securities and Exchange Commission. Any forward-looking statements represent the Company's views only as of the date of this press release. The Company anticipates that subsequent events and developments may cause its views to change. While the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so except as required by law.

References

1. U.S. Food and Drug Administration. "Guidance for Industry: Expedited Programs for Serious Conditions - Drugs and Biologics, 2014". Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expedited-programs-serious-conditions-drugs-and-biologics. Last accessed: November 16, 2022.

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