Alkeus Pharmaceuticals Receives FDA Rare Pediatric Disease and Fast Track Designations for Gildeuretinol as a Treatment for Stargardt Disease

- Designations underscore significant unmet need in Stargardt disease, a rare and serious pediatric disease for which no treatment exists.

- Data from Alkeus' TEASE program were presented at the American Academy of Ophthalmology's 2024 annual meeting.

- Alkeus plans to apply for a Priority Review Voucher along with its NDA submission.

CAMBRIDGE, Mass., November 18, 2024 -- Alkeus Pharmaceuticals, Inc., a biopharmaceutical company dedicated to preserving the sight of individuals impacted by retinal diseases, today announced that gildeuretinol (ALK-001), an investigational oral therapy, has received Rare Pediatric Disease and Fast Track designations from the U.S. Food and Drug Administration (FDA) for the treatment of Stargardt disease.

"Stargardt disease is a serious and relentlessly progressive rare condition leading to severe vision loss in children and adults, and there is no approved treatment available," said Michel Dahan, President and CEO of Alkeus Pharmaceuticals. "Receiving both the FDA's Rare Pediatric Disease and Fast Track designations are important milestones for Alkeus that highlight the potential for oral gildeuretinol to be a groundbreaking therapy for patients. These designations were granted on top of the previously awarded Breakthrough Therapy and Orphan Drug designations. Together, these achievements recognize the significant unmet medical need in Stargardt disease and the overwhelming burden on patients as well as their families and caregivers."

The FDA grants Rare Pediatric Disease designation to therapeutics intended to treat serious or life-threatening rare diseases in which the serious manifestations primarily affect individuals from birth to 18 years of age. With this designation, Alkeus may be eligible to receive a priority review voucher (PRV) upon approval that could be used to advance another clinical development program. Fast Track designation is granted by the FDA to facilitate the development and expedite the review of drugs intended to treat a serious condition that has clinical data demonstrating the potential to address an unmet medical need. Gildeuretinol has previously received Breakthrough Therapy and Orphan Drug designations from the FDA.

Data from Alkeus' TEASE program in Stargardt disease were most recently presented during the 2024 American Academy of Ophthalmology annual meeting in October by Christine Nichols Kay, M.D., of Vitreo Retinal Associates in Gainesville, Fla.

In TEASE-1, a placebo-controlled, double-masked, randomized 24-month study in patients with Stargardt disease, gildeuretinol slowed the growth rate of atrophic retinal lesions area (square root) by 21.6% compared to untreated patients during the two-year study. Gildeuretinol also demonstrated a 29.5% reduction in growth rate of atrophic lesions in a sensitivity analysis using non-transformed values. The growth rates of atrophic retinal lesions were 0.18 mm/year (0.87 mm^2/year untransformed area) in the gildeuretinol treated arm, and 0.23 mm/year (1.23 mm^2/year) in the untreated arm, mean difference 0.05 mm/year with 95% confidence interval, 0.03 to 0.07, $p<0.001$. The difference was 0.36 mm^2/year using non-transformed analysis with 95% confidence interval, 0.23 to 0.50, $p<0.001$.

In addition, Dr. Kay presented interim data from the TEASE-3 study demonstrating that early-stage Stargardt disease patients treated with gildeuretinol showed no disease progression and remained asymptomatic while on therapy for between two and six years. Gildeuretinol treatment in early-stage Stargardt patients was associated with relatively stable visual acuity.

“TEASE-1 is the first randomized, controlled trial in Stargardt disease that has shown an efficacy endpoint, which is very exciting as an inherited retinal disease specialist taking care of patients with this devastating condition,” said Dr. Kay. “In addition, the TEASE-3 data indicate the potential value of treating patients with Stargardt disease as early as possible, before onset of progressive central vision loss.”

In both TEASE-1 and TEASE-3, gildeuretinol demonstrated a favorable safety and tolerability profile. There were no adverse events related to hyper- or hypo-vitaminosis A such as xerophthalmia, chromatopsia, dark adaptation delays or night blindness.

Stargardt disease is a serious cause of severe vision impairment in children and young adults, with an estimated 30,000 to 87,000 people affected in the U.S. There is no approved treatment. In individuals with Stargardt disease, the ABCA4 protein is defective. This defect in the protein results in the accelerated dimerization of vitamin A, forming toxic by-products that irreversibly damage the retina, resulting in progressive vision loss.

About the TEASE Program

The Tolerability and Effects of ALK-001 on Stargardt diseasE (TEASE) studies consist of four independent clinical studies of oral gildeuretinol (ALK-001) in Stargardt disease, denoted as TEASE-1, TEASE-2, TEASE-3 and TEASE-4. The TEASE-1 study was a randomized, double-masked, placebo-controlled trial in 50 patients with Stargardt disease. Gildeuretinol met its prespecified primary efficacy endpoint showing a 21.6% reduction in the growth rate of retinal atrophic lesions area (square root) ($p<0.001$), and a 29.5% reduction for untransformed areas of retinal atrophic lesions against untreated patients. Gildeuretinol was well-tolerated. The TEASE-2 trial is an ongoing, fully enrolled, randomized, double-masked, placebo-controlled trial in 80 patients with moderate Stargardt disease, expected to read out topline data in 2025. TEASE-3, the first clinical trial in early-stage Stargardt disease, is an open-label study of gildeuretinol in genetically confirmed patients with early signs of disease visible on retinal imaging, but who

have not begun experiencing symptoms of vision loss. TEASE-4 is an open-label extension study.

About Gildeuretinol Acetate (ALK-001)

Oral gildeuretinol acetate (ALK-001) is a new chemical entity designed to reduce the dimerization of vitamin A without modulating the visual cycle. In preclinical studies, gildeuretinol decreased vitamin A dimerization down to the normal rate and prevented retinal degeneration and loss of visual function in animals with Stargardt disease. A randomized, placebo-controlled, double-masked clinical trial of gildeuretinol in late-stage Stargardt patients (TEASE-1) showed clinically and statistically significant slowing of the growth of retinal lesions over two years of treatment. Additional clinical trials of gildeuretinol in Stargardt disease are ongoing. Gildeuretinol has received Breakthrough Therapy, Rare Pediatric Disease, Fast Track and Orphan Drug designations for Stargardt disease from the U.S. Food and Drug Administration. A study (SAGA) of gildeuretinol in 198 patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD) demonstrated a meaningful trend in the reduction of lesion growth rate and demonstrated a functional benefit in low luminance visual acuity (LLVA). In studies, gildeuretinol demonstrated a favorable safety and tolerability profile.

About Alkeus Pharmaceuticals

Alkeus Pharmaceuticals, Inc. is a private biopharmaceutical company with headquarters in Cambridge, Mass., backed by institutional investors led by Bain Capital Life Sciences. Founded in 2010, Alkeus is developing therapies for serious diseases of the eye with high unmet need, with the purpose to protect the sight of individuals impacted by retinal diseases. Alkeus' breakthrough-designated lead candidate, gildeuretinol acetate (ALK-001), is a new chemical entity currently being evaluated in clinical trials for the treatment of Stargardt disease and for geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

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