FOR IMMEDIATE RELEASE

Topline Results from Alkeus Pharmaceuticals' Study of Oral Gildeuretinol Demonstrate Significant Trend in Slowing GA Progression and Visual Function Improvement

- Oral gildeuretinol demonstrated a statistically significant reduction in the geographic atrophy (GA) lesion growth rate of 15.3% from 6 to 24 months (p=0.047) in a pre-specified analysis.

- Gildeuretinol is the first investigational oral therapy to demonstrate a functional benefit in low luminance visual acuity (LLVA) over 24 months (p=0.031), a key secondary endpoint.

- Gildeuretinol showed a clinically meaningful reduction in GA lesion growth rate of 13.4% from baseline to 24 months (p=0.075), the study's primary endpoint.

- Results indicate that slowing the formation of toxic vitamin A dimers could help address the high unmet need for oral therapies in multiple retinal diseases.

- Gildeuretinol demonstrated a favorable safety and tolerability profile. Among participants at risk of developing Choroidal Neovascularization (CNV) or wet AMD, only 11% in the gildeuretinol group experienced these adverse events compared to 44% in the placebo group, as reported by clinical investigators.

CAMBRIDGE, Mass., October 23, 2024 – Alkeus Pharmaceuticals, Inc., a biopharmaceutical company dedicated to preserving the sight of individuals impacted by retinal diseases, today announced that patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD) treated with investigational oral therapy gildeuretinol (ALK-001) showed a statistically significant reduction in the GA lesion growth rate of 15.3% vs. placebo from 6 to 24 months (p=0.047). Gildeuretinol also demonstrated a statistically significant visual function improvement, showing 4.4 fewer letters lost (p=0.031) in low luminance visual acuity (LLVA) over 24 months. Gildeuretinol showed a clinically meaningful trend in slowing GA growth rate of 13.4% from baseline to 24 months (p=0.075), the study's primary endpoint. A trend toward functional benefit in best corrected visual acuity (BCVA) was demonstrated with 3.3 fewer letters lost (p=0.099).

Topline results of the SAGA study of gildeuretinol for the treatment of GA secondary to AMD were presented by Alexander Melamud, M.D., M.A., retina specialist and vitreoretinal surgeon with the Retina Group of Washington and a principal investigator in the SAGA study during the 128th Annual Meeting of the American Academy of Ophthalmology (AAO) held in Chicago October 18-21, 2024.

“These data indicate a significant slowing of the growth rate of GA lesions, as well as reducing visual function decline,” said Seemi Khan, M.D., M.P.H., M.B.A., Chief Medical Officer of Alkeus Pharmaceuticals. “It takes a couple of months for gildeuretinol to replace vitamin A and achieve a therapeutic effect. Therefore, we are encouraged by the sensitivity analysis measuring the effect starting at six months of treatment. These data represent the first clinical demonstration that slowing vitamin A dimerization could be a target in the treatment of GA secondary to AMD. By slowing dimerization with gildeuretinol’s unique mechanism, we could reduce further damage to the retina at more advanced stages and possibly delay or prevent the onset of GA. We are excited by the potential of gildeuretinol as an oral therapy with functional benefits in GA, in addition to its potential to be the first therapy for Stargardt disease. We would like to thank the patients, investigators and trial sites for their participation in this study, as well as the National Institutes of Health National Eye Institute for providing funding for this study.”

SAGA was a 24-month, double-masked, randomized, placebo-controlled trial to investigate the safety, pharmacokinetics, tolerability and efficacy in patients with GA secondary to AMD. The study enrolled 198 patients. The primary efficacy endpoint was the growth rate of GA lesions from baseline to 24 months as assessed by Fundus Autofluorescence (FAF). The first key secondary endpoint was the change in LLVA from baseline to 24 months.

A favorable safety and tolerability profile was demonstrated by gildeuretinol, consistent with prior clinical studies of gildeuretinol in Stargardt disease. Additionally, among participants at risk of developing Choroidal Neovascularization (CNV) or wet AMD, only 11% in the gildeuretinol group experienced these adverse events compared to 44% in the placebo group, as reported by the retina specialist investigators.

“These data are meaningful and changing the conversation in the space about what might be possible with next generation treatments for patients with GA and earlier stages of AMD,” said Charles Wykoff, M.D., Ph.D., retina specialist and Director of Research at Retina Consultants of Texas. “While the primary endpoint was not met, the anatomic efficacy signal appears real, and most interestingly there appears to be a consistent signal of functional preservation with treatment. This patient population could benefit tremendously from a safe and effective systemic treatment option.”

GA is a serious, progressive condition that causes irreversible loss of central vision. It is estimated that the median time of progression to severe visual impairment is slightly over six years. There is no oral therapy approved by the FDA to treat GA. The prevalence of GA in the United States is estimated to be over 1 million people, with 160,000 new cases occurring each year.

“One of the most exciting aspects of these results is that gildeuretinol is the first oral medication to show a meaningful positive effect on low luminance visual acuity in macular degeneration,” Dr. Melamud said. “One of the first things patients lose in macular degeneration is low light vision, which can have a dramatic impact on daily living. The positive effect demonstrated on LLVA is significant. Based on these results, this therapy would definitely have a place in the

overall strategy of treating AMD and slowing the decline observed in our patients. The favorable safety profile could warrant treatment as early as possible."

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 designation and orphan drug designation 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).

For further information, please contact:

Media Relations
media@alkeuspharma.com
Website: www.alkeuspharma.com