KYOWA KIRIN

News release

Kyowa Kirin Announces Topline Results from Phase 2 Global Study of KHK4951 Eye Drops for Neovascular Age-Related Macular Degeneration

- KHK4951 evaluated as a non-invasive maintenance therapy approach following anti-VEGF treatment in patients with nAMD -

- Approximately 70% of patients did not experience a loss of 15 or more letters in BCVA through Week 52, although the primary endpoint was not met -

- Generally well tolerated with no new safety signals identified -

Tokyo, Japan, September 8, 2026 -- Kyowa Kirin Co., Ltd. (TSE:4151, President and CEO: Abdul Mullick, "Kyowa Kirin") today announced topline results from its Phase 2 global clinical study (4951-002) of KHK4951, an investigational nanocrystal ophthalmic suspension containing tivozanib, a tyrosine kinase inhibitor (TKI) targeting vascular endothelial growth factor receptors (VEGFR)-1, -2 and -3, in patients with neovascular age-related macular degeneration (nAMD). KHK4951 is being developed as a non-invasive maintenance therapy approach following anti-VEGF treatment.

Across all three KHK4951 dose groups, approximately 65% to 69% of patients avoided the primary composite event of a loss of 15 or more letters in best-corrected visual acuity (BCVA) or the need for rescue treatment through Week 52. The study did not demonstrate superiority of the high-dose group over the low-dose group and therefore did not meet its primary endpoint. Among patients who completed the study, mean BCVA and central subfield thickness (CST) were generally maintained. KHK4951 was generally well tolerated, and no new safety signals were identified.

These findings provide clinically relevant evidence to inform the potential role of an eye drop-based maintenance strategy in nAMD, while the absence of a true control group and the lack of a dose-response signal require careful interpretation and further study.

Clinical Study Overview

Study 4951-002 was a multicenter, randomized, double-masked Phase 2 trial in patients with nAMD. The study evaluated the efficacy and safety of KHK4951 as maintenance therapy in patients who demonstrated a favorable response during a run-in period with intravitreal anti-VEGF treatment.

Key study elements included:

- Patients received three intravitreal injections of aflibercept 2 mg prior to randomization.
- Patients were randomized to KHK4951 0.5% once daily (QD), 2.0% once daily (QD), or 2.0% twice daily (BID).（QD; once daily), BID; twice daily）
- The study was designed to evaluate efficacy, safety, and dose regimen selection to support future development.
- The primary endpoint was the comparison of treatment groups for the proportion of patients experiencing either a loss of 15 or more letters in best-corrected visual acuity (BCVA) or requiring rescue treatment between Week 8 and Week 52.

Efficacy Results:

Although approximately 65% to 69% of participants across all treatment groups maintained their vision within 15 letters decrease in BCVA, no statistical difference was observed between the high-dose group (2.0% BID) and low-dose group (0.5% QD), which was evaluated as the primary endpoint, and as a result, the primary endpoint was not met.

Additional findings observed in the study included:

- The proportion of patients experiencing either a loss of 15 or more letters in visual acuity or requiring rescue treatment at Week 52 was 31.8% in the 0.5% QD group, 34.9% in the 2.0% QD group, and 31.1% in the 2.0% BID group.
- Kaplan-Meier analyses showed that approximately 62% to 67% of patients did not experience 15 or more letters increase in BCVA or require rescue treatment between Week 8 and Week 52.
- Among study completers, BCVA and CST were generally maintained throughout the study period.

The results provide important scientific insights into maintenance therapy approaches for nAMD and may contribute to future development considerations in this therapeutic area.

Safety Results:

KHK4951 was generally well tolerated across the dose range evaluated.
Key safety findings included:

- KHK4951 was generally well tolerated at doses up to 2.0% BID.
- No new safety signals were identified during the study.
- Dry eye and punctate keratitis were observed in some patients.
- No clinically meaningful trend in blood pressure elevation, a potential concern associated with systemic VEGF inhibition, was observed.

" The interim results from the KHK4951-002 study provide important insights and support further investigation," said Dante Pieramici, M.D., Medical Director of Clinical Research, California Retina Consultants, Santa Barbara, CA, USA. "Although the lack of a true control group remains a key limitation and necessitates careful interpretation, it is encouraging that many patients maintained visual outcomes over an extended period following initial anti-VEGF treatment. For patients with neovascular age-related macular degeneration, the burden of frequent intravitreal injections continues to be a significant challenge in clinical practice. In this context, evaluating a topical therapeutic approach represents an important area of research that may expand future treatment options. While additional studies are needed to further assess these findings, the results support the continued clinical development of KHK4951 and contribute to ongoing efforts to address the needs of patients living with retinal diseases."

"In this study, many patients across all dose groups, including the low-dose group, maintained their vision over the approximately one-year observation period. Among patients who completed the study, mean BCVA, a key measure of visual function, remained generally stable," said Yoshifumi Torii, M.D., Ph.D., Chief Medical Officer of Kyowa Kirin. "While the study did not demonstrate the predefined dose-response relationship, important insights were obtained from anatomical assessments, including central subfield thickness (CST), as well as from the overall safety evaluation of the program. nAMD is a chronic condition that often requires long-term treatment and may place a substantial burden on patients, caregivers, and healthcare providers. We believe these findings contribute valuable knowledge regarding future maintenance treatment strategies. Kyowa Kirin remains committed to carefully evaluating the knowledge gained from this study as we continue our efforts to bring innovative treatment options to people living with nAMD."

The Kyowa Kirin Group companies strive to contribute to the health and well-being of people around the world by creating new value through the pursuit of advances in life sciences and technologies.

About KHK4951

The active ingredient of KHK4951, tivozanib, is a small-molecule vascular endothelial growth factor receptor (VEGFR)-1, -2 and -3 tyrosine kinase inhibitor discovered by Kyowa Kirin. KHK4951 is a novel nanocrystallized eye drop formulation designed to efficiently deliver tivozanib to posterior segment tissues and is being developed as a potential treatment option for neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME). Through this program, Kyowa Kirin is exploring a non-invasive therapeutic approach that may complement the current standard of care for patients requiring long-term disease management. Preclinical studies demonstrated efficient drug delivery to posterior ocular tissues through nanocrystal technology[1], and results from the Phase 1 study supported further clinical development. KHK4951 has not been approved in any country or region, and its safety and efficacy have not been established.

About Neovascular Age-Related Macular Degeneration (nAMD)

Neovascular age-related macular degeneration (nAMD) is a chronic retinal disease characterized by the formation of abnormal blood vessels beneath the macula, which may lead to progressive vision loss and blindness. Overall, age-related macular degeneration (AMD) is estimated to affect approximately 200 million people worldwide, and this number is projected to increase to approximately 290 million by 2040 as populations continue to age. Although nAMD accounts for only a subset of AMD cases, it is known as a major cause of severe vision impairment. In Japan, more than 100,000 patients are estimated to be living with nAMD, and the number of patients is expected to increase further as the population ages. The current standard of care is intravitreal injection of anti-VEGF agents; however, the need for continuous hospital visits and repeated administration may place a significant burden on patients, caregivers and healthcare systems.

About Kyowa Kirin

Kyowa Kirin aims to discover novel medicines with life-changing value. As a Japan-based Global Specialty Pharmaceutical Company, we have invested in drug discovery and biotechnology innovation for more than 70 years and are currently working to engineer the next generation of antibodies and cell and gene therapies with the potential to help patients affected by a severe or rare disease. A shared commitment to our values, to sustainable growth, and to making people smile unites us across our three regions – JAPAC, North America, and EMEA. You can learn more about the business of Kyowa Kirin at: https://www.kyowakirin.com/

Reference

[1] K. Satake, S. Koshiba, H. Haniuda, T. Amano, M. Hiura, T. Ishii, S. Horita. Preclinical Ocular Pharmacokinetics and Efficacy of Novel Tivozanib Eye Drops for Neovascular Age-Related Macular Degeneration. Invest Ophthalmol Vis Sci . 2026 Jul 1;67(8):55.

Note 1. Best Corrected Visual Acuity (BCVA)

Best Corrected Visual Acuity (BCVA) is a standard measure of visual function assessed under optimal vision correction, such as with eyeglasses or contact lenses. It is commonly used in clinical trials of retinal diseases, including neovascular age-related macular degeneration (nAMD), to evaluate changes in a patient's ability to see over time.

Note 2. Central Subfield Thickness (CST)

Central Subfield Thickness (CST) is a measurement of retinal thickness in the central macula obtained by optical coherence tomography (OCT). In nAMD, fluid leakage from abnormal blood vessels may lead to retinal thickening. CST is therefore widely used to evaluate disease activity, anatomical changes in the retina, and the biological activity of investigational treatments in clinical studies.