

Topline Results of the KHK4951 Phase 2 study in nAMD patients

September 9th, 2026

Chief Medical Officer (CMO) Yoshifumi Torii

Kyowa Kirin Co., Ltd.

NCT06116890



This document contains forward-looking statements regarding the outlook, targets, plans, and other future-related matters of the Company (including its consolidated subsidiaries in Japan and overseas). These statements are based on our reasonable judgments using current information and forecasts but involve uncertainties that could cause actual results to differ materially.

These uncertainties include, but are not limited to, risks inherent in the domestic and international pharmaceutical industry, intellectual property rights, side effects, legal regulations, product defects, fluctuations in raw material/fuel prices, market prices, and exchange/financial markets.

This document is for investor information purposes only and contains information on pharmaceuticals (including products under development), but it is not intended for promotional advertising or medical advice.

Vision 2030

Kyowa Kirin will realize the successful creation and delivery of life-changing value* that ultimately makes people smile, as a Japan-based Global Specialty Pharmaceutical company built on the diverse team of experts with shared passion for innovation.

Provide pharmaceuticals for unmet medical needs

We are focused on developing medicines for diseases where there is a clear patient need for new options. We make full use of multiple therapeutic modalities, including biotechnology such as antibody technology, and beyond, building on our Kyowa Kirin established strengths.

Address patient-centric healthcare needs

By applying scientific insights and cutting-edge technologies cultivated through our pharmaceutical business, we aim to create new value that focuses on the needs of people living with diseases.

We will continue to meet society's medical needs through patient-centered innovation.

Retain the trust of society

We pursue world-class product quality and operational excellence to grow our business in ways which build long-term trust with our stakeholders

* Make patients smile through dramatic improvements in quality of life by identifying the unmet medical needs of people battling with medical conditions and by creating and supplying new drugs or services that help them overcome those challenges.

KHK4951

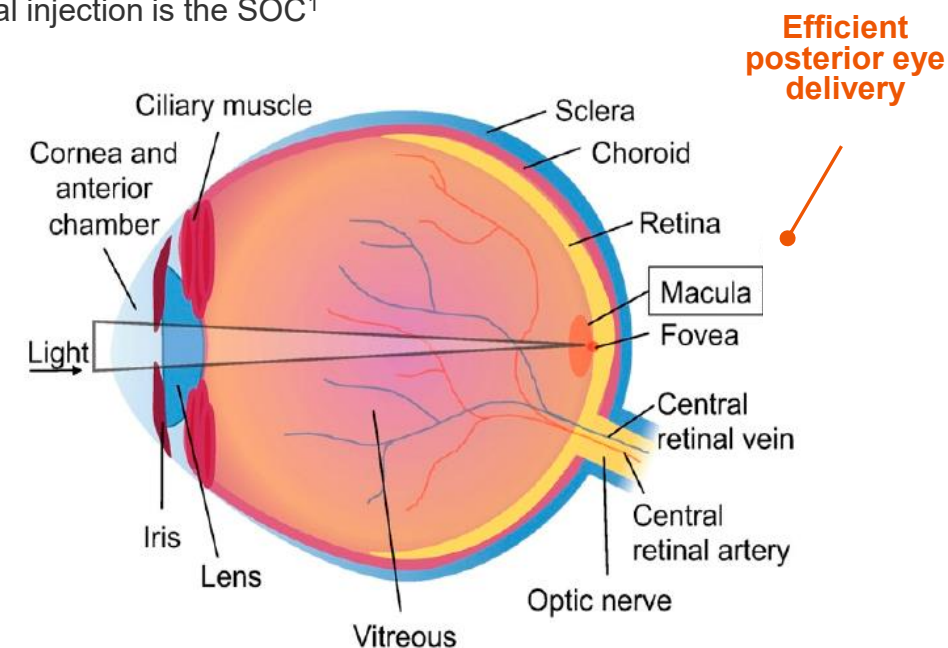
In development for neovascular Age-related Macular Degeneration (nAMD) and Diabetic Macular Edema (DME)
Pursuing the potential to deliver the first anti-VEGF eye drop treatment for diseases where intravitreal injection is the SOC¹



KHK4951



Nano-crystallized
tivozanib



Market Potential | nAMD

Global

Patients
2670k

Existing Market Size²
1 Trillion Yen~

Market Potential | DME

Global

Patients
2220k

Existing Market Size²
500B~1T yen



Disease areas

Ophthalmology



Modalities

Small Molecule
(Eye drop)



Commercialization

Exploring
Strategic Partner

KHK4951 Phase 2 Summary of Test Results

Achieved the company's pre-defined product profile targets

Results suggest the potential of an eye drop-centered maintenance treatment strategy

Effectiveness

In all treatment groups, including the low-dose group, **65-69% of subjects maintained their vision within 15 letters decrease in BCVA without any rescue IVT¹ injection at Week 52**

Primary Evaluation Items

The "statistical difference among dose groups in the proportion of patients with a reduction of 15 or more BCVA² between 8 and 52 weeks" was not observed

Safety and Tolerability

No new safety signals were observed in this study

Secondary Evaluation Items

In all groups, BCVA and CST³ remained stable throughout the treatment period.

1. IVT = Intravitreal; 2. Best-Corrected Visual Acuity; 3. Central Subfield Thickness

Clinical Needs for Eye Drop Maintenance Therapy in nAMD

01

Diseases requiring ongoing treatment

nAMD requires ongoing intravitreal injection therapy with anti-VEGF agents and follow-up to maintain long-term vision

02

Burden of current treatment

Treatment with intravitreal injections places a significant burden on patients and healthcare professionals, including repeated injections, regular visits to specialized medical institutions, patient mobility, and support



The vision the KHK4951 aims for

Developing maintenance treatment centered on eye drops after induction with intravitreal injections (maintaining visual acuity, reducing IVT injection count, and providing rescue treatment only when necessary)

The Concept of KHK4951 as Eye Drop Maintenance Therapy

Current Maintenance Therapy by Intravitreal Injection

- Focusing on extending the interval between intravitreal injections
- Repeated procedures at specialized centers are necessary
- The burden of injections and hospital visits continues

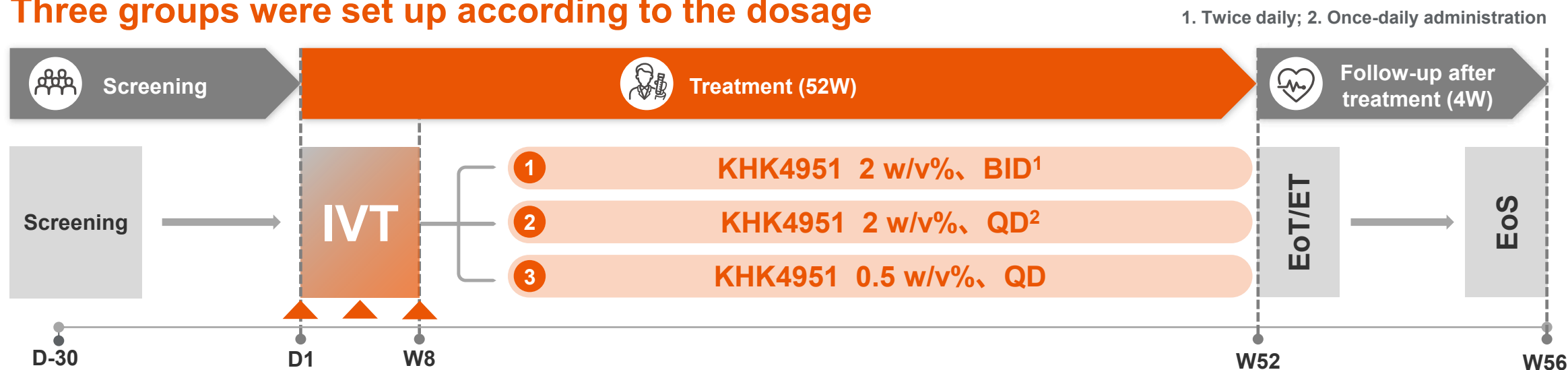


Maintenance Therapy Models Examined in KHK4951

- Maintenance therapy mainly involves daily eye drops
- Daily self-management and professional rescue treatment as needed
- Potential to reduce the number of injections and the burden of visiting clinics

KHK4951 Design of Phase 2 Trials

Three groups were set up according to the dosage



Overview	
Research Objectives	- Evaluating the efficacy and safety of KHK4951 at different doses - Determining the optimal KHK4951 dose for the Phase 3 study
Primary Evaluation Items	Evaluation of superiority of KHK4951 high dose to low dose: Statistically significant difference in the proportion of patients who lost 15 or more BCVA letters between W8 and W52
Eligible Patients	- Treatment-naïve patients - Patients previously treated with anti-VEGF agents
Sample size	132 patients receiving KHK4951 treatment (no placebo arm)

Approximately 65–69% of cases in all treatment groups maintained their vision within 15 letters decrease in BCVA without any rescue IVT injection

- 15 or more letters decrease in BCVA: **31.1% (2.0% BID), 34.9% (2.0% QD), 31.8% (0.5% QD)**
- No significant differences were observed among dose groups, and the primary endpoint was not met

	KHK4951 0.5 w/v% QD (N = 44)	KHK4951 2.0 w/v% QD (N = 43)	KHK4951 2.0 w/v% BID (N = 45)
Participants Meeting Criteria	14	15	14
Proportion with Exact 95% CI (%)	31.82 (18.610, 47.578)	34.88 (21.008, 50.927)	31.11 (18.166, 46.649)
Difference (%) vs. 0.5 w/v% QD (Reference Dose)	—	3.07	-0.71
Adjusted Difference (%) (Stratified Newcombe 95% CI)	—	2.35 (-17.040, 21.558)	-0.43 (-19.213, 18.360)
p-value	—	NA	0.965

Mean change in BCVA during the KHK4951 dosing period

In all groups, the mean BCVA remained stable from the KHK4951 administration. No clear differences were observed in the mean BCVA change among dose groups.

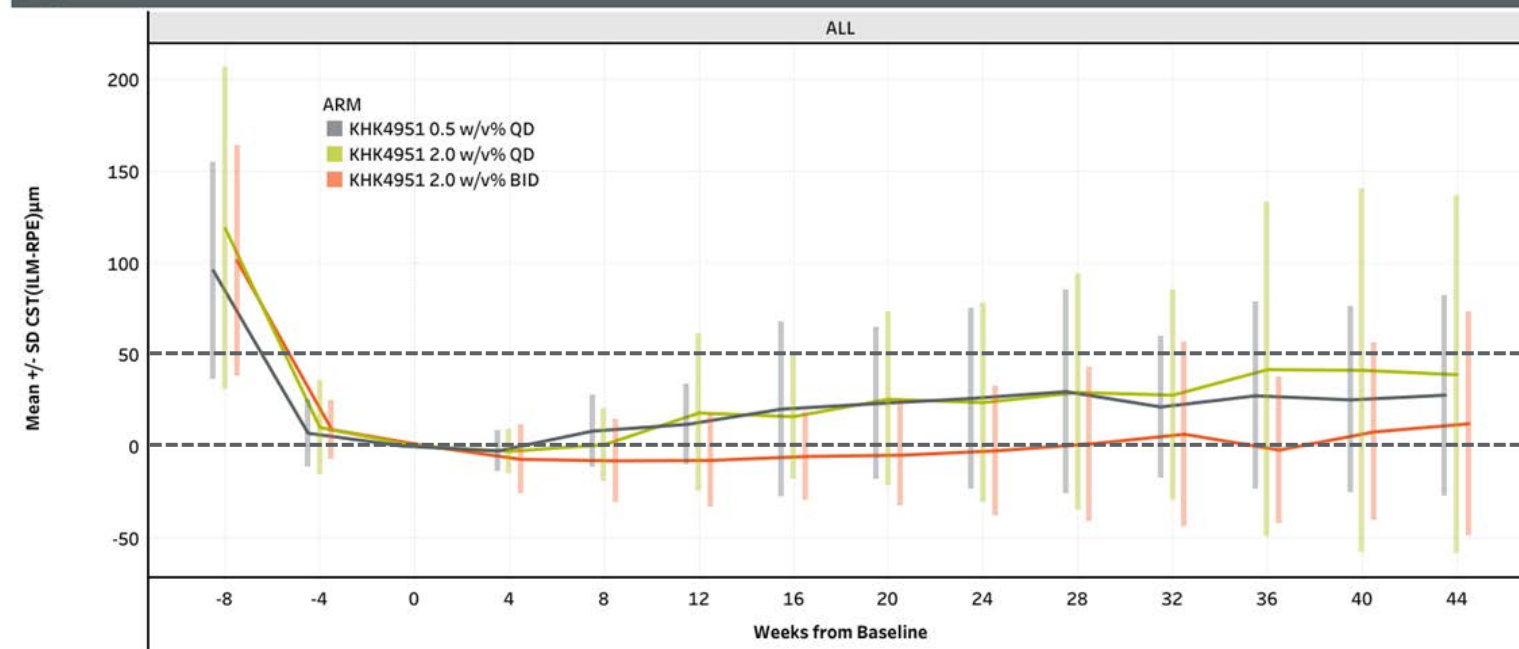


Mean change in CST during the KHK4951 dosing period

In all groups, the mean CST remained stable from the KHK4951 administration. Meanwhile, no clear differences were observed in the mean CST change among dose groups.

Plot of Mean $\pm$ SD CST(ILM-RPE)(μ m) Over Time(ITT)

Change from Analysis Baseline
N = 132



		-W8	-W4	W0	W4	W8	W12	W16	W20	W24	W28	W32	W36	W40	W44
n	0.5 w/v% QD	44	43	44	44	42	37	38	36	34	33	30	29	28	27
	2.0 w/v% QD	43	43	43	39	40	38	36	32	30	29	29	25	24	23
	2.0 w/v% BID	45	42	45	40	39	38	36	31	33	30	29	28	26	25

ILM: Internal Limiting Membrane
RPE: Retinal pigment epithelium

Safety and Tolerability

No new safety signals were observed in this study

Parameter	Main findings
Ocular site	A small number of dry eyes and punctate keratitis were mainly observed in the 2.0% BID cohort
Systemic	No significant new safety signals observed during KHK4951 treatment (e.g., increase in blood pressure)
Study completion	About 70% completed the study. The main reasons for study discontinuation were the need for alternative treatments or progression of nAMD (about 15%)

Clinical Perspectives on Eye-Drop Maintenance Therapy — KOL Comments

KOLs	Feedbacks
Dr. Pieramici 	Although the absence of a true control group is the study's primary limitation, making it difficult to attribute the observed outcomes directly to the drug, Dr. Pieramici noted that approximately 70% of patients maintained vision (lost less than 3 lines vision or needed rescue) after induction therapy, which may be better than expected from observation alone.
Dr. Iida 	- Dr. Iida agreed Kyowa Kirin's interpretation that this result shows therapeutic effect of KHK4951. - Based on Ph2 result, Ph3 plan should be carefully considered. At this time, non-inferiority study to aflibercept 2 mg with appropriate rescue criteria is reasonable for Ph3 study.
Dr. Murata 	- It is exceeded our expectations that 70% of participants maintained their vision through Week 52 without any intravitreal anti-VEGF injections. This suggests that KHK4951 showed a therapeutic effect. - Even if there is a dose-dependent increase in the frequency of adverse events, these are manageable and acceptable compared to the invasiveness of intravitreal anti-VEGF injections.

Summary and Conclusion

Achieved the company's pre-defined product profile targets

Results suggest the potential of an eye drop-centered maintenance treatment strategy

Efficacy Evaluation

Approximately 65–69% of subjects maintained their vision within 15 letters decrease in BCVA without any rescue IVT injection at Week 52

No difference was observed among dose groups; the primary endpoint was not met

Secondary Endpoints

In all groups, BCVA and CST remained stable throughout the treatment period.

Potential for New Treatment Strategies

Presenting the potential of a maintenance therapy strategy centered on eye drops that could help reduce the burden on patients and healthcare professionals.

Based on the insights gained from this exam, our company will explore various options to maximize the value of this program

Kyowa Kirin continuously creates Life-changing value by leveraging disease science and drug discovery technology

From Story for Vision 2030

Disease Science

Deeply Exploring Unmet Medical Needs (UMN) of Diseases, Their Causes, and Mechanisms

- Exploring treatment possibilities starting from unmet patient needs

KHK4951: Focusing on UMN in patients with maintenance therapy that does not rely on frequent intravitreal injections

Drug Discovery Technology

Application of the optimal modality for achieving treatment

- Combining research and formulation technology expertise to verify treatment concepts in clinical practice

KHK4951: Pursuing efficient posterior-segment delivery using nanocrystallized tivozanib



**Creating
Life-changing
value**

KHK4951: Strategic Partnering Assets

Assets beyond our focus areas – Maximizing value through collaboration with partners



~Contact for Inquiries Regarding This Material~

Kyowa Kirin Co., Ltd.
Finance Dep., IR Group
+81-3-5205-7206 / ir@kyowakirin.com