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(translation)

Notice of Application for Domestic Manufacturing and Marketing Approval for K-232
Treatment for Glaucoma and Ocular Hypertension (Ripasudil hydrochloride hydrate and
Brimonidine tartrate fixed combination eye drop)

With regard to the rho-kinase (Note 1) inhibitor Ripasudil hydrochloride hydrate discovered by D. Western Therapeutics Institute, Inc. (DWTI) and licensed out to Kowa Co., Ltd., DWTI today received notification that Kowa has submitted an application to Japan's Ministry of Health, Labour and Welfare for the approval of domestic manufacturing and marketing of K-232, a fixed combination eye drop containing Ripasudil hydrochloride hydrate and Brimonidine tartrate (Note 2), as a treatment for glaucoma and ocular hypertension (Note 3).

K-232 is the world's first fixed combination eye drop containing a combination of Ripasudil hydrochloride hydrate, the active ingredient in the rho-kinase inhibitor GLANATEC® Ophthalmic Solution 0.4%, and the α 2-adrenergic agonist Brimonidine tartrate. Since the drug has a different pharmacological point of action from existing combination eye drops, it can be used in combination with various other treatments for glaucoma and ocular hypertension.

Phase III clinical trials for K-232 have been ongoing in Japan since February 2020. The trials have confirmed that, when used alone or in combination with existing drug treatments for glaucoma and ocular hypertension, the drug has the effect of further lowering intraocular pressure and that it is safe. Judging from standard cases, DWTI anticipates that the approval review will be completed in about one year.

Polypharmacy is poised to become the standard treatment for glaucoma. K-232 is expected to improve patient adherence, and DWTI believes that the drug can contribute to the treatment of glaucoma patients.

As DWTI does not plan to receive any milestone payment from this latest development, there will be no impact on results for the fiscal year ending December 2021. If the drug is approved and launched, however, DWTI will receive contractual royalties from Kowa. We believe this will contribute to improving our medium- and long-term performance.

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Explanation of terms

(Note 1) Rho kinase

Rho kinase is one of the family of protein phosphorylation enzymes (protein kinases), and is involved in the control mechanism of various cellular responses via the Rho-ROCK pathway.

(Note 2) Brimonidine tartrate

Eye drops containing Brimonidine tartrate as an active ingredient act on the α_2 -adrenergic receptor, and demonstrate effectiveness in lowering intraocular pressure by suppressing aqueous humor production and promoting aqueous humor outflow through the uveoscleral route. The drug is marketed in many countries, including the U.S., as an eye drop for patients with glaucoma and ocular hypertension.

(Note 3) Glaucoma and ocular hypertension

Glaucoma is a disease marked by distinctive changes to the optic nerves and visual field. It is characterized by functional and structural abnormalities of the eye, wherein optic nerve damage can normally be improved or contained by sufficiently lowering intraocular pressure. If left untreated, symptoms may range from narrowing of the visual field to blindness. Glaucoma is the number one cause of adult-onset blindness in Japan (2005). Ocular hypertension is a condition in which intraocular pressure exceeds normal levels although there is no narrowing of the visual field. Currently, the only reliable, evidence-based treatment for glaucoma is lowering intraocular pressure. Drug treatments are the first choice for treating primary open-angle glaucoma (in a broad sense).