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June 30, 2025

To whom it may concern:

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Notification of Approval in Singapore for Glaucoma and Ocular Hypertension Treatment "GLA-ALPHA<sup>®</sup> Combination Ophthalmic Solution (Japanese product name)"

D. Western Therapeutics Institute, Inc. (hereafter, "DWTI") hereby announces that on June 25, 2025, Kowa Co., Ltd., to which DWTI out-licensed its in-house discovered Rho-kinase<sup>1</sup> inhibitor ripasudil hydrochloride hydrate, obtained marketing approval in Singapore of the glaucoma and ocular hypertension<sup>2</sup> treatment "GLA-ALPHA<sup>®</sup> Combination Ophthalmic Solution" (development code: K-232; generic name: ripasudil hydrochloride hydrate/brimonidine tartrate<sup>3</sup>)" (hereafter, "this drug"), a new fixed combination eye drop.

This drug is the world's first fixed combination eye drop containing ripasudil hydrochloride hydrate, the active pharmaceutical ingredient in Rho-kinase inhibitor GLANATEC<sup>®</sup> ophthalmic solution  $0.4\%^4$ , and  $\alpha$ 2-adrenergic agonist brimonidine tartrate. Since the drug has a different site of action than existing combination eye drops, it can be used in combination with various other treatments for glaucoma and ocular hypertension.

Kowa has been marketing this drug in Japan since December 2022, and sales are steadily increasing. Since receiving approval in Japan, Kowa has been considering overseas sales, and had already approved in Thailand. Kowa is continuing to consider further overseas expansion.

Once this product is launched in Singapore, DWTI will receive royalties based on the license agreement it entered with Kowa.

By providing Thai patients with a new treatment option, we believe that this product will contribute to the control of intraocular pressure, which is important in the treatment of glaucoma and ocular hypertension, and will help to improve adherence in patients who require multiple eye drops.

Although no milestone payments will be triggered by this event, and this development will have no impact on DWTI's earnings results for the fiscal year ending December 2025, we believe it will contribute to improving earnings in the longer term.

#### 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) 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. 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).

## (Note 3) Brimonidine tartrate

Eye drops containing brimonidine tartrate as an active ingredient act on the  $\alpha$ 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 4) GLANATEC® Ophthalmic Solution 0.4%

GLANATEC<sup>®</sup> Ophthalmic Solution 0.4% was launched by Kowa in December 2014. This product is an eye drop preparation with a novel mechanism of action, the first of its kind in the world, for treating glaucoma and ocular hypertension. The drug lowers intraocular pressure by inhibiting Rho kinase, a type of protein kinase, and promoting the outflow of aqueous humor from the main collector channel via the trabecular meshwork/Schlemm's canal.