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To Whom It May Concern,

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Title and Name of Representative: Ryo Kubota

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**Kubota Vision Inc. Initiates Clinical-Grade GMP Drug Substance Manufacturing for Emixustat Hydrochloride for the Compassionate Use Program in France**

Kubota Vision Inc. ("Kubota Vision"), a wholly-owned subsidiary of Kubota Pharmaceutical Holdings Co., Ltd. (Headquarters: Minato-ku, Tokyo, Japan; Founder, Chairman, President and CEO: Ryo Kubota, MD, PhD; hereinafter referred to as "the Company") today announced that the drug substance manufacturing process for emixustat hydrochloride ("emixustat") has been successfully transferred to a new manufacturing site. Kubota Vision will initiate the manufacture of a full-scale, clinical-grade good manufacturing practice ("GMP") batch of drug substance in April 2026 in order to support the compassionate use program in France.

This follows [the March 2, 2026 announcement](#) regarding the supply and licensing agreement between Kubota Vision and Laboratoires KÔL ("KÔL") for a Stargardt disease treatment candidate under compassionate use authorization in France.

As previously announced, under that agreement Kubota Vision is responsible for the procurement of raw materials, manufacture of the drug substance serving as the active pharmaceutical ingredient ("API"), manufacture of the final packaged drug product (oral tablet) of emixustat, and regulatory review activities, while KÔL is responsible for activities in France other than manufacturing, including local storage, distribution, local interactions with the French National Agency for Medicines (ANSM), and certain medical affairs activities.

The successful technology transfer of the drug substance manufacturing process and the initiation of a full-scale, clinical-grade GMP drug substance batch represent an important operational milestone in supporting the



compassionate use program in France. Kubota Vision will continue to work with relevant parties to ensure quality and supply readiness and to advance the development and business activities for emixustat.

At this time, the impact of this matter on the Company's financial results is expected to be minimal. If any matters requiring disclosure arise in the future, the Company will promptly make an announcement.

### **About Stargardt disease (STGD1)**

Stargardt disease (STGD1) is a rare hereditary retinal disorder that typically develops in childhood or adolescence and causes gradual loss of vision. It is also known as Stargardt macular dystrophy or juvenile macular degeneration. The condition is primarily caused by mutations in the ABCA4 gene, which lead to progressive damage of the photoreceptor cells and subsequent decline in visual acuity. Patients with Stargardt disease may experience a range of symptoms, including loss of visual field, color vision abnormalities, distortion, blurriness, and difficulty seeing in the central field of vision. While typical cases appear in childhood or adolescence, some patients may not notice symptoms until adulthood.

The retina, located at the back of the eye, supports a mechanism called the visual cycle, which converts light into electrical signals that allow the brain to perceive images. In this cycle, light is absorbed by a visual pigment composed of retinal (a form of vitamin A) and a protein called opsin within the photoreceptor cells. The light-induced structural change of this pigment activates intracellular signaling pathways, altering the membrane potential and transmitting the resulting signal to the brain.

During this visual cycle, toxic vitamin A-derived byproducts are generated as a result of light absorption. When these harmful substances accumulate within the retinal pigment epithelium (RPE) cells, they cause cellular dysfunction and apoptosis (cell death), ultimately leading to the loss of photoreceptor cells, resulting in progressive vision loss or blindness. The accumulation of these toxic metabolites within RPE cells is considered the direct pathological cause of Stargardt disease.

In a healthy retina, a membrane transport protein removes these toxic precursors from photoreceptor cells, protecting the RPE cells from damage. In Stargardt disease, however, mutations in the ABCA4 gene, which encodes the ABCR membrane transporter essential to this process in the visual cycle, impair this function. These gene mutations are regarded as the fundamental cause of the disease.

Currently, no approved treatment is available for Stargardt disease.



### **About Emixustat**

Emixustat is expected to suppress the progression of Stargardt disease (STGD1) by selectively inhibiting RPE65, a key enzyme in the visual cycle, through our group's proprietary visual cycle modulation (VCM) technology. This selective inhibition reduces the accumulation of metabolic waste products generated during the visual cycle.

Visual cycle modulation (VCM) technology is a therapeutic approach designed to reduce the accumulation of toxic byproducts in the retina that are generated through the visual cycle—a biological process in the retina that converts light into electrical signals. This technology is expected to mitigate retinal damage caused by oxidative stress and protect the retina from light-induced injury. As retinal pigment epithelium (RPE) cells mature, they continuously phagocytose the outer segments of photoreceptors at a steady rate, while simultaneously accumulating toxic byproducts from the visual cycle. When Emixustat hydrochloride is applied to the visual system, it selectively targets rod cells without affecting cone cells and suppresses the production of key enzymes involved in the visual cycle. By inhibiting enzyme production, Emixustat reduces rod cell activity and slows the accumulation of toxic byproducts in RPE cells. By modulating (slowing down) the visual cycle, the buildup of these harmful byproducts is reduced, thereby delaying disease progression.

### **About Laboratoires KÔL**

Laboratoires KÔL is a French specialty pharmaceutical company focused on ophthalmology, with a strong emphasis on corneal and rare diseases. The company possesses deep expertise in corneal grafting, access authorization pathways (AAC/AAP), and preventive eye-care therapies, pioneering innovative treatments for rare corneal disorders. Drawing inspiration from ancient eye-care traditions such as Egyptian “khôl” and integrating cutting-edge medical science, Laboratoires KÔL collaborates with hospitals, research institutions, and regulatory bodies to deliver patient-centric therapeutic solutions worldwide. The company engages in the research, development, manufacturing, and commercialization of ophthalmic drugs, with a particular focus on corneal graft rejection, corneal neovascularization, and retinal disease. Its proprietary antisense oligonucleotide platform, is developed into 2 different eyedrops formulations respectively for corneal disease (Olisens®), and retina. A large clinical program is on-going for this antiangiogenic messenger RNA technology with preliminary promising results in both indications. For more information, visit [laboratoires-kol.com/en\\_GB](http://laboratoires-kol.com/en_GB).

### **About Kubota Vision Inc.**

Kubota Vision Inc. is a wholly owned subsidiary of Kubota Pharmaceutical Holdings Co., Ltd. (Tokyo 4596), committed to translating innovation into a diverse portfolio of drugs and devices to preserve and restore vision for millions of people worldwide. Kubota Pharmaceutical Group's research and development pipeline includes Emixustat hydrochloride as a therapeutic candidate for Stargardt disease (STGD1) and proliferative diabetic



retinopathy (PDR), as well as a VAP-1 inhibitor targeting Alzheimer's disease and metabolic dysfunction-associated steatohepatitis (MASH). As medical device and related product portfolio includes Kubota Glass®, a wearable device designed to suppress the progression of myopia, and eyeMO®, a retinal monitoring device developed for home- and tele-ophthalmology use. eyeMO® is designed to support patients with wet age-related macular degeneration (AMD) and diabetic macular edema (DME) as part of a comprehensive Patient-Based Ophthalmology Suite (PBOS) aimed at enabling advanced, patient-centered ophthalmic care. In addition, the Group is developing a swept-source optical coherence tomography (SS-OCT) device for spaceflight-associated neuro-ocular syndrome (SANS) under a development contract with NASA/TRISH. Kubota Glass® is currently being marketed in both the Japanese and Chinese markets, further expanding the Kubota Pharmaceutical Group's commitment to advancing ophthalmic innovation and accessible vision care solutions globally. For more information, visit [kubotavision.com](http://kubotavision.com)

The "Kubota" logo is registered trademark of Kubota Pharmaceutical Holdings Co., Ltd.

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