Bayer Yakuhin, Ltd.
Santen Pharmaceutical Co., Ltd.

Intravitreal VEGF Inhibitor EYLEA® approved as a Treatment of Neovascular Glaucoma (NVG), its fifth indication

Osaka, March 25, 2020 – Bayer Yakuhin, Ltd. (Osaka, hereinafter Bayer Yakuhin) and Santen Pharmaceutical Co., Ltd. (Osaka, hereinafter Santen) announced today that Bayer Yakuhin has received approval for the additional indication of "neovascular glaucoma (NVG)" for the intravitreal VEGF* inhibitor EYLEA® solution for intravitreal injection 40 mg/mL (aflibercept [genetical recombination], hereinafter EYLEA®) and EYLEA® intravitreal injection KIT 40 mg/mL, pre-filled syringe to administer EYLEA® (hereinafter EYLEA® pre-filled syringe). Orphan Drug Designation has been granted for this indication.

* VEGF = vascular endothelial growth factor

EYLEA® vial and EYLEA® pre-filled syringe have received approvals for age-related macular degeneration with subfoveal choroidal neovascularization, macular edema secondary to retinal vein occlusion, choroidal neovascularization in pathologic myopia and diabetic macular edema. This approval is the fifth indication EYLEA® obtained.

NVG is a secondary glaucoma in which new blood vessels are formed in the iris and the anterior chamber angle. The outflow of aqueous humor is inhibited and, intraocular pressure is increased. NVG is a serious complication mainly in diseases causing retinal ischemia such as proliferative diabetic retinopathy and central retinal vein occlusion. There remains a high unmet medical need as progressive disease is likely to lead to blindness.

Dr. Masaru Inatani, Professor at Department of Ophthalmology, Faculty of Medical Sciences, University of Fukui said, "NVG is an intractable glaucoma that tends to lead to blindness, so it demands urgent treatment. Up to this point, there wasn't any approved treatment directly acting on VEGF, a major cause of neovascularization, to regress new blood vessels and reduce intraocular

pressure. EYLEA®'s approval for use in Japan for NVG, the first in the world, presents a new treatment option for patients in Japan. The clinical use of EYLEA®, which is expected to reduce intraocular pressure, is anticipated to be beneficial not only to patients but also to healthcare professionals."

Santen is responsible for distributing EYLEA® in Japan, while Bayer Yakuhin holds the marketing authorization for the product. Both companies jointly conduct detailing activities at medical institutions and provide information about the product to medical professionals.

EYLEA® pre-filled syringe is currently under preparation for the launch.

<Product Overview >

(The addition is indicated in underlined letters.)

Product name	EYLEA® solution for IVT inj. 40 mg/mL EYLEA® IVT inj. KIT 40 mg/mL
Non-proprietary name	Aflibercept (genetical recombination)
Indication	Age-related macular degeneration with subfoveal choroidal neovascularization Macular edema secondary to retinal vein occlusion Choroidal neovascularization in pathologic myopia Diabetic macular edema Neovascular glaucoma
Dosage & administration	**Age-related macular degeneration with subfoveal choroidal neovascularization** The initial dosage of Aflibercept (Genetical Recombination) is 2 mg (0.05 mL) administered by intravitreal (IVT) injection once every month for 3 times consecutively (initial phase). In the subsequent maintenance phase, it is usually administered intravitreally once every 2 months. The dosing interval may be adjusted according to the patient's symptoms, but it should be ≥1 month. **Macular edema secondary to retinal vein occlusion, Choroidal neovascularization in pathologic myopia** The dosage of Aflibercept (Genetical Recombination) is 2 mg (0.05 mL) administered by IVT injection. The dosing interval should be ≥1 month.

	Diabetic macular edema The dosage of Aflibercept (Genetical Recombination) is 2 mg (0.05 mL), administered by IVT injection once every month for 5 times consecutively. Then, it is usually administered intravitreally once every 2 months. The dosing interval may be adjusted according to the patient's symptoms, but it should be ≥1 month. **Neovascular glaucoma** The dosage of Aflibercept (Genetical Recombination) is 2 mg (0.05 mL) administered by IVT injection. Retreatment with Aflibercept may be performed if necessary, with a dosing interval of ≥1 month.
Date of marketing authorization	September 28, 2012
Date of additional approval	Macular edema secondary to central retinal vein occlusion November 22, 2013 Choroidal neovascularization in pathologic myopia September 19, 2014 Diabetic macular edema November 18, 2014 Macular edema secondary to retinal vein occlusion June 26, 2015 Neovascular glaucoma March 25, 2020
Marketing authorization held by	Bayer Yakuhin, Ltd.
Distributed by	Santen Pharmaceutical Co., Ltd.

About VEGA study and VENERA study

This approval is based on the data from two Phase III studies: the randomized, double-blind, controlled VEGA study, and the open-label, single-arm VENERA study to investigate the efficacy, safety, and tolerability of intravitreal EYLEA® in Japanese patients with NVG. Taken together, both studies showed efficacy of EYLEA® as assessed by the change from baseline in intraocular pressure at Week 1 as the primary endpoint and the proportion of subjects with improvement from baseline in the grade of neovascularization of iris (NVI) at Week 1 as the secondary endpoint. Also, adverse event findings during both studies were consistent with the known safety profile for EYLEA®.

About VEGF and EYLEA® (aflibercept solution for injection into the eye)

Vascular Endothelial Growth Factor (VEGF) is a naturally occurring protein in the body. Its normal role in a healthy organism is to trigger formation of new blood vessels (angiogenesis) supporting the growth of the body's tissues and organs. It is also associated with the growth of abnormal new blood vessels in the eye, which exhibit abnormal increased permeability that leads to edema.

EYLEA® is a recombinant fusion protein, consisting of portions of human VEGF receptors 1 and 2 extracellular domains fused to the Fc portion of human IgG1 and formulated as an iso-osmotic solution for intravitreal administration. EYLEA® acts as a soluble decoy receptor that binds VEGF-A and Placental Growth Factor (PGF) and thereby can inhibit the binding and activation of their cognate VEGF receptors.

Bayer and Regeneron Pharmaceuticals, Inc. are collaborating on the global development of EYLEA®. Regeneron maintains exclusive rights to EYLEA® in the U.S. Bayer has licensed the exclusive marketing rights outside the U.S., where the companies share equally the profits from sales of EYLEA®, except for Japan where Regeneron receives a percentage of net sales.

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About Bayer

Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. Its products and services are designed to benefit people by supporting efforts to overcome the major challenges presented by a growing and aging global population. At the same time, the Group aims to increase its earning power and create value through innovation and growth. Bayer is committed to the principles of sustainable development, and the Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2019, the Group employed around 104,000 people and had sales of 43.5 billion euros. Capital expenditures amounted to 2.9 billion euros, R&D expenses to 5.3 billion euros. For more information, go to www.bayer.com.

About Bayer Yakuhin, Ltd.

Bayer Yakuhin, Ltd., headquartered in Osaka, is a healthcare company which combines business activities of Pharmaceuticals, Consumer Health and Animal Health (companion and farm animal products). Pharmaceuticals business is focused on the following areas: Cardiovascular & Neurology, Oncology & Hematology, Women's Healthcare, Ophthalmology and Radiology. Bayer Yakuhin aims to be one of leading pharmaceutical companies, which responds to Japanese patients' unmet medical needs. More information is available at www.byl.bayer.co.jp/.

About Santen

As a specialized company dedicated to ophthalmology, Santen carries out research, development, marketing, and sales of pharmaceuticals, over-the-counter products, and medical devices. Santen is the market leader for prescription ophthalmic pharmaceuticals in Japan, and its products now reach patients in more than 60 countries. With scientific knowledge and organizational capabilities nurtured over a nearly 130-year history, Santen provides products and services to contribute to the well-being of patients, their loved ones and consequently to society. For more information, please visit Santen's website (www.santen.com).

Forward-Looking Statements of Bayer

This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.

Forward-Looking Statements of Santen

Information provided in this press release contains forward-looking statements. The achievement of these forecasts is subject to risk and uncertainty from various sources. Therefore, please note that the actual results may differ significantly from the forecasts. Business performance and financial conditions are subject to the effects of changes in regulations made by the governments of Japan and other nations concerning medical insurance, drug pricing and other systems, and to fluctuations in market variables such as interest rates and foreign exchange rates.