News Release

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

Intravitreal VEGF Inhibitor “EYLEA” Obtains Additional Indication of Diabetic Macular Edema (DME), its Fourth Indication

Osaka, November 18, 2014 – 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 “diabetic macular edema (DME)” for the intravitreal VEGF* inhibitor EYLEA® solution for intravitreal injection 40 mg/mL and EYLEA® intravitreal injection KIT 40 mg/mL (aflibercept [genetical recombination], hereinafter EYLEA). EYLEA has received approvals for age-related macular degeneration with subfoveal choroidal neovascularization (wet AMD: wet age-related macular degeneration) and macular edema secondary to central retinal vein occlusion (CRVO) and myopic choroidal neovascularization (mCNV). This approval is the fourth indication the drug obtained.

* VEGF = vascular endothelial growth factor

This approval was based on the one-year data from the phase 3 VIVID-DME and VISTA-DME trials of 862 patients, which compared EYLEA 2 milligrams (mg) given monthly, 2 mg given every two months (after five initial monthly injections), or macular laser photocoagulation (at baseline and then as needed). In the DME studies, after one year, the mean changes in best-corrected visual acuity (BCVA), as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) eye chart for the monthly and every two month treatment arms, were statistically significantly improved compared to the control group and were similar to each other. Across both trials, patients in both EYLEA arms, on average, the ability to read approximately two additional lines on an eye chart compared with almost no change in the control group.

"Diabetic retinopathy (DR) is one of the three major complications of diabetes, which is increasing worldwide, and is the second cause[1] of visual impairment in Japan," said Dr. Hiroko Terasaki, the

Professor at Department of Ophthalmology, Nagoya University Graduate School of Medicine, and the Steering Committee member of the VIVID-DME trial, in which Japan has also participated. "DME, which is estimated to account for approximately 20%[2] of DR, has a risk of severe vision loss. Phase 3 trials have demonstrated that EYLEA provides a statistically significant outcome as compared to laser treatment. This approval is expected to be great news for patients with diabetes, as EYLEA becomes a treatment option that may improve vision in DME patients."

Based on the co-promotion agreement for EYLEA in Japan concluded on May 7, 2012, Santen distributes the product. Bayer Yakuhin and Santen both provide EYLEA drug information to healthcare professionals.

<Overview of EYLEA® solution for intravitreal (IVT) injection (inj.) 40 mg/mL>
(The addition is indicated in underlined letters.)

Product name	EYLEA® solution for IVT inj. 40 mg/mL
Non-proprietary name	Aflibercept (genetical recombination)
Indication	Age-related macular degeneration with subfoveal choroidal neovascularization Macular edema secondary to central retinal vein occlusion Myopic choroidal neovascularization Diabetic macular edema
Dosage & administration	**Age-related macular degeneration with subfoveal choroidal neovascularization** 2 mg of Aflibercept (Genetical Recombination) (0.05 mL) is administered by intravitreal injection once every month for three times consecutively (initiation phase). In the following maintenance phase, usually, it is administered by intravitreal injection once every 2 months. The dosing interval may be adjusted according to the patient's symptoms and conditions, however, it should e one month or longer.** **Macular edema secondary to central retinal vein occlusion, Myopic choroidal neovascularization** The injection dose is 2 mg Aflibercept (Genetical Recombination) [equivalent to 0.05 mL EYLEA solution] per injection, administered by intravitreal injection. The dosing interval should be one month or longer. **Diabetic macular edema** The injection dose is 2mg Aflibercept (Genetical Recombination)

	(0.05mL), administered by intravitreal injection. Eylea treatment is initiated with one intravitreal injection per month for five consecutive doses. Thereafter the recommended treatment is usually one intravitreal injection every 2 months. The dosing interval may be adjusted according to the patient's symptoms and conditions, however, it should be one month or longer. **Added to align with other indiations
Date of marketing authorization	September 28, 2012
Date of additional approval	Macular edema secondary to central retinal vein occlusion November 22, 2013 Myopic choroidal neovascularization September 19, 2014 Diabetic macular edema November 18, 2014
Marketing authorization held by	Bayer Yakuhin, Ltd.
Distributed by	Santen Pharmaceutical Co., Ltd.

About the Phase 3 study results

In the VIVID-DME study conducted in Europe, Japan and other countries, patients receiving aflibercept solution for injection 2 mg every other month (after 5 initial monthly injections) had a mean gain from baseline in BCVA of +10.7 letters, at Week 52. Patients receiving laser photocoagulation had a mean change from baseline in BCVA of +1.2 letters. Additionally, at Week 52, 53.3 % of patients receiving aflibercept solution for injection 2 mg every other month achieved an increase of at least 10 letters from baseline compared to the laser treatment group with 25.8% achieving a similar gain.

In the VISTA-DME study conducted in the United States, patients receiving aflibercept solution for injection 2 mg every other month (after 5 initial monthly injections) had a mean gain from baseline in BCVA of +10.7 letters, at Week 52, compared to patients receiving laser photocoagulation who had a mean change from baseline in BCVA of +0.2 letters. Additionally, at Week 52, 58.3% of patients receiving aflibercept solution for injection 2 mg every other month achieved an increase of at least 10 letters from baseline compared to the laser treatment group with 19.5% achieving a similar gain.

About Diabetic Macular Edema (DME)

Diabetic macular edema (DME) and diabetic retinopathy (DR) are common microvascular complications in people with diabetes. DR is a disease affecting the blood vessels of the retina. DME occurs when fluid leaks into the center of the macula, the light-sensitive part of the retina responsible for sharp, direct vision. Fluid in the macula can cause severe vision loss or blindness.

Visual impairment due to DME is estimated to affect approximately 3% of people with diabetes and is therefore the most frequent cause of blindness in young and mid-aged adults in most developed countries. As the incidence of diabetes has been steadily climbing, it is projected that the number of people impacted by DME will also grow.

About EYLEA® (aflibercept solution for injection)

EYLEA is a novel intravitreal VEGF inhibitor co-developed by Bayer HealthCare in Germany and Regeneron Pharmaceuticals, Inc., in the United States for the treatment of retinal disorders. It is a recombinant fusion protein consisting of portions of the extracellular domains of human VEGF receptors 1 and 2 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 for various members of the VEGF family including VEGF-A and placental growth factor (PlGF) and binds with them with high affinity and thus can inhibit the binding and activation of these cognate VEGF receptors. EYLEA thus inhibits abnormal vascularization and leakage.

EYLEA has been approved in many countries worldwide for wet age-related macular degeneration (wet AMD), and DME. The approval in Japan in September is the world-first approval of the drug for the treatment of myopic choroidal neovascularization (mCNV), while regulatory submission has been made also in Asia Pacific region. Furthermore, the drug has been approved for retinal vein occlusion (RVO) in the United States. In Europe and Japan, it has been approved for macular edema secondary to central retinal vein occlusion (CRVO) and regulator submission has been made based on the phase 3 data from macular edema secondary to branch retinal vein occlusion (BRVO).

Bayer HealthCare and Regeneron Pharmaceuticals, Inc. are collaborating on the global development of EYLEA. Regeneron maintains exclusive rights to EYLEA in the United States. Bayer HealthCare licensed the exclusive marketing rights outside the United States, where the

companies share equally the profits from sales of EYLEA, except for Japan where Regeneron receives a royalty on net sales.

References:

1 Sato, R, et al.: Research Committee on Chorioretinal Degenerations and Optic Atrophy, the Ministry of Health, Labour and Welfare of Japan, 2012

2 Nakano, S. The 114th Annual Meeting of the Japanese Ophthalmological Society, 2010

About Santen
Founded in 1890, Santen is a global company headquartered in Osaka, Japan. Santen researches, develops and markets ophthalmic products for physicians worldwide. Among prescription ophthalmic pharmaceuticals, Santen holds the top share within the Japanese market and is one of the leading ophthalmic companies worldwide. For more information, please visit http://www.santen.co.jp/

About Bayer Yakuhin
Bayer Yakuhin Ltd., headquartered in Osaka, is a healthcare company which combines business activities of Pharmaceuticals, Consumer Care, Radiology & Interventional and Animal Health (companion and farm animal products). Pharmaceuticals business is focused on the following areas: Cardiovascular & Neurology, Oncology & Hematology, Women's Healthcare and Ophthalmology. Bayer Yakuhin aims to be one of leading pharmaceutical companies, which responds to Japanese patients' unmet medical needs, with the spirit of Bayer's corporate slogan "Science For A Better Life".
Bayer Yakuhin homepage: http://www.bayer.co.jp/byl

About Bayer HealthCare
The Bayer Group is a global enterprise with core competencies in the fields of health care, agriculture and high-tech materials. Bayer HealthCare, a subgroup of Bayer AG with annual sales of EUR 18.9 billion (2013), is one of the world's leading, innovative companies in the healthcare and medical products industry and is based in Leverkusen, Germany. The company combines the global activities of the Animal Health, Consumer Care, Medical Care and Pharmaceuticals divisions. Bayer HealthCare's aim is to discover, develop, manufacture and market products that will improve human and animal health worldwide. Bayer HealthCare has a global workforce of 56,000 employees (Dec 31, 2013) and is represented in more than 100 countries. Find more information at www.bayerhealthcare.com.

About Regeneron Pharmaceuticals
Regeneron is a leading science-based biopharmaceutical company based in Tarrytown, New York that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. Regeneron markets medicines for eye diseases, colorectal cancer, and a rare inflammatory condition and has product candidates in development in other areas of high unmet medical need, including hypercholesterolemia, oncology, rheumatoid arthritis, asthma, and atopic dermatitis. For additional information about the company, please visit www.regeneron.com.

Bayer Forward-Looking Statements
This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer Group or subgroup 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.

Santen Forward-looking Statements
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.