



News Release

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

Intravitreal VEGF Inhibitor “EYLEA” Obtains Additional Indication of Myopic Choroidal Neovascularization (mCNV)

Osaka, September 22, 2014 – Bayer Yakuhin, Ltd. (Osaka, hereinafter Bayer Yakuhin) and Santen Pharmaceutical Co., Ltd. (Osaka, hereinafter Santen) announced that Bayer Yakuhin has received approval for the additional indication of myopic choroidal neovascularization (mCNV) 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) on September 19, 2014. 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).” This approval is the third indication the drug obtained. The approval in Japan is the world-first approval of the drug for the treatment of mCNV.

* VEGF = vascular endothelial growth factor

mCNV is a disease of the retina where new, abnormal blood vessels grow into the retina in persons who are severely myopic and have pathological changes in the back of the eye, which may lead to visual impairment. In a majority of patients of pathological myopia¹ that develops mCNV, their visual acuity can be severely reduced within few years to approximately 10 years, if left untreated.

As severe myopia is particularly common in Asia, Bayer HealthCare conducted the Phase 3 MYRROR study, a multinational clinical trial in Japan and other Asian countries, in mCNV which occurs as a complication of severe myopia. In MYRROR study, patients received EYLEA had a mean improvement in best corrected visual acuity from baseline at week 24 of 12.1 letters, compared to a loss of 2 letters in patients received sham injections ($p < 0.0001$). EYLEA was

started with a single injection; additional injections were given only in case of newly occurring or persisting mCNV. In the EYLEA arm, patients received in the first quarter of the study, i.e. from baseline to week 12, a median of 2 injections. In each of the following three quarters, the median of injections was 0. These data show the disease can be successfully managed with acute treatment regimen (only a few numbers of injections in a short-term treatment period). Furthermore, the efficacy gains seen at week 24 were maintained and even extended further in the EYLEA arm until week 48. On the other hand, all patients in the sham injection arm received EYLEA at week 24, followed by EYLEA injections based on retreatment criteria until week 48, but a mean improvement in best corrected visual acuity from baseline at week 48 for this arm was only 3.9 letters.

Dr. Tatsuro Ishibashi, Professor of Department of Ophthalmology at Kyushu University, and the principal investigator of the Phase 3 MYRROR study said, “The group of patients who received delayed administration of EYLEA showed poorer improvements in visual acuity than the group of patients who received EYLEA from the beginning of the trial. This indicates the significance of the early treatment. It would be a great benefit for mCNV patients, many of who are of working age, that EYLEA is now approved as a new effective treatment option in mCNV, as the drug shows great therapeutic outcomes already in the area of wet AMD.”

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 <u>Myopic choroidal neovascularization</u>
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

	<p>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</p> <p>Macular edema secondary to central retinal vein occlusion, Myopic choroidal neovascularization</p> <p>The injection dose is 2 mg Aflibercept (Genetical Recombination) [equivalent to 0.05mL EYLEA solution] per injection, administered by intravitreal injection. The dosing interval should be one month or longer.</p>
Date of marketing authorization	September 28, 2012
Date of additional approval	<p>Macular edema secondary to central retinal vein occlusion: November 22, 2013</p> <p><u>Myopic choroidal neovascularization</u> <u>September 19, 2014</u></p>
Marketing authorization held by	Bayer Yakuhin, Ltd.
Distributed by	Santen Pharmaceutical Co., Ltd.

About Phase 3 MYRROR Program

MYRROR was a double-masked, sham-controlled trial that randomized 122 patients to receive either aflibercept 2 mg or sham. Patients in the active treatment arm received one initial 2 mg dose of aflibercept. Patients were evaluated every 4 weeks and were eligible to receive additional aflibercept 2 mg intravitreal injections determined by visual and anatomic criteria, through 20 weeks. Patients on the sham arm received monthly sham injections through week 20. Starting at week 24, patients in both arms were eligible to receive aflibercept 2 mg on as needed basis through week 48. The primary endpoint of the study was the mean change at week 24 from baseline in best-corrected visual acuity (BCVA) as measured on the Early Treatment Diabetic Retinopathy Scale (ETDRS) eye chart, a standard chart used in research to measure visual acuity.

About Myopic Choroidal Neovascularization (mCNV)

mCNV is a disease of the retina where new, abnormal blood vessels grow into the retina in persons who are severely myopic (typically more than minus six diopters²) and have pathological changes in the back of the eye. The disease is characterized by an abnormally elongated eye with a physical stretching of the sclera, choroid, and retina resulting in degenerative and progressive

changes. These degenerative changes can incite the development of choroidal neovascularization. Anti-VEGF treatment has been shown to be effective in wet age-related macular degeneration (wet AMD), which is also characterized by a growth of new, abnormal blood vessels in the retina. Severe myopia is particularly common in Asia. mCNV is associated with high degrees of myopia and leads to progressive vision loss. In a majority of patients of pathological myopia that develops mCNV, their visual acuity can be severely reduced within few years to approximately 10 years, if left untreated. In East Asia, the prevalence of myopia is significantly higher than in West Asia, and appears to have an earlier onset. In Japan, pathologic myopia is the second most common cause of blindness³.

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 for the treatment of wet age-related macular degeneration (wet AMD) and for the treatment of macular edema secondary to central retinal vein occlusion (CRVO). It has also been approved for the treatment of diabetic macular edema (DME) in Europe and the United States, and regulatory submission has been made in Asia Pacific region including Japan and Latin America. The approval in Japan is the world-first approval of the drug for the treatment of mCNV, while regulatory submission has been made also in Asia Pacific region. Furthermore, regulatory submission has been made in Europe, the United States, and Japan for the treatment of visual impairment due to macular edema secondary to branch retinal vein occlusion.

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.

[Notes]

1 Conditions with pathological changes such as atrophy and degeneration in retina or choroid following extension in the posterior segment of the eye among severe myopia with extended axial length of eye ball

2 Unit of refractive power of lenses

3 Reference: "Prevalence of Visual Impairment in the Adult Japanese Population by Cause and Severity and Future Projections" (Ophthalmic Epidemiology, 17(1), 50-57, 2010, Copyright 2010 Informa UK, Ltd.)

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.com>

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.