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Investor News

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Treatment of macular edema secondary to branch retinal vein occlusion (BRVO):

Bayer Submits New Application for Aflibercept Solution for Injection into the Eye in Japan Based on Phase 3 Data in Patients with BRVO

Aflibercept Solution for Injection met primary endpoint of the Phase 3 VIBRANT study

Leverkusen, Germany, September 4, 2014 – Bayer HealthCare today announced that Bayer Yakuhin, Ltd., Osaka, Japan, has submitted an application for marketing authorization for aflibercept solution for injection into the eye, based on the Phase 3 VIBRANT trial in patients with macular edema secondary to branch retinal vein occlusion (BRVO). Aflibercept solution for injection into the eye has already been approved in Japan under the brand name EYLEA® for the treatment of patients with neovascular age-related macular degeneration (wet AMD) and the treatment of macular edema secondary to central retinal vein occlusion (CRVO). Marketing authorization applications have also been submitted in Japan for the treatment of choroidal neovascularization secondary to pathologic myopia (myopic CNV) and for the treatment of diabetic macular edema (DME).

“BRVO is a common retinal vascular disorder with an estimated 14 million people affected worldwide. In Japan, approximately 2.0% of residents over the age of 40 are estimated to have BRVO. It is a severe disease which may lead to permanent vision loss if the macular edema is not treated appropriately,” said Dr. Erik Louvel, Head of Product Development of Bayer Yakuhin. “This submission which is the fifth application for aflibercept solution for injection in Japan reinforces the commitment of Bayer to improving outcomes for the millions of patients suffering from a broad range of vision-threatening retinal diseases.”

The submission is based on the positive results from the data collected in Japan as part of the Phase 3 VIBRANT trial. In the VIBRANT study, 53% of patients who received aflibercept solution for injection 2 milligram (mg) monthly gained at least 15 letters

(equivalent to three lines) in best corrected visual acuity (BCVA) from baseline at week 24, the primary endpoint of the study, compared to 27% of patients who received laser, the current standard of care ($p<0.001$). In addition, aflibercept solution for injection met a key secondary endpoint, achieving a 17.0 letter mean improvement over baseline in BCVA compared to a 6.9 letter mean improvement in patients who received laser ($p<0.0001$).

Aflibercept solution for injection into the eye was generally well tolerated. Through week 24, the most common ocular adverse events in patients treated with aflibercept solution for injection were conjunctival hemorrhage and eye pain. The incidence of serious adverse events (SAE) was 9.9% in the aflibercept solution for injection group and 9.8% in the laser group. Up to week 24, one death and one Anti-Platelet Trialists' Collaboration (APTC) defined event (non-fatal stroke) occurred during the trial, both events occurred in patients in the laser group. There were no cases of intraocular inflammation. There was one ocular SAE in a patient in the aflibercept solution for injection group, which was a traumatic cataract.

About the Phase 3 VIBRANT Study

VIBRANT was a Phase 3, randomized, double-masked, active-controlled 52-week study, with approximately 60 study sites in Japan and North America, comparing aflibercept solution for injection 2 mg monthly with laser photocoagulation in subjects with macular edema secondary to BRVO. The primary endpoint was the proportion of subjects who gained at least 15 letters in BCVA from baseline at week 24, as measured on the Early Treatment Diabetic Retinopathy Scale (ETDRS) eye chart, a standard chart used in research to measure visual acuity. At week 24, patients initially randomized to aflibercept solution for injection 2 mg monthly continued with dosing every two months, while those initially randomized to receive laser continued as is unless they qualified for rescue therapy (aflibercept solution for injection 2 mg monthly for 3 months, followed by dosing every other month through week 52).

About Branch Retinal Vein Occlusion (BRVO)

BRVO is a common retinal vascular disorder and a significant cause of visual impairment affecting around 14 million people worldwide. Previous research in Hisayama, Japan, showed that 2.0% of residents over the age of 40 had BRVO. Of the two main types of retinal vein occlusion (RVO) – CRVO and BRVO – the latter is more common with prevalence four times higher than that of CRVO. In BRVO, one or more branches of the

main blood vessel draining the retina are blocked, resulting in the release of vascular endothelial growth factor and consequent retinal edema.

About VEGF and 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.

Aflibercept solution for injection 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. Aflibercept acts as a soluble decoy receptor that binds VEGF-A and placental growth factor (PlGF) and thereby can inhibit the binding and activation of their cognate VEGF receptors.

Aflibercept solution for injection into the eye has been approved under the brand name EYLEA® in almost 80 countries for the treatment of patients with neovascular age-related macular degeneration (wet AMD) and around 60 countries for the treatment of visual impairment due to macular edema secondary to central retinal vein occlusion (CRVO). The eye drug is also approved for the treatment of diabetic macular edema (DME) in over 30 countries. Over 2 million doses of the eye drug have been administered since launch. For BRVO, application for marketing authorization have also been submitted in Europe and the U.S. In Japan and Asia Pacific, Aflibercept solution for injection into the eye has also been submitted for approval to the health authorities for the treatment of choroidal neovascularization secondary to pathologic myopia (myopic CNV).

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

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. More information is available at www.healthcare.bayer.com.

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