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Investor News

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Aflibercept solution for injection into the Eye:

Bayer Receives positive CHMP Opinion for the Treatment of Visual Impairment due to Diabetic Macular Edema in EU

Leverkusen, Germany, June 27, 2014 – Bayer HealthCare today announced that aflibercept solution for injection into the eye has been recommended for approval by the European Committee for Medicinal Products for Human Use (CHMP) for the treatment of visual impairment due to diabetic macular edema (DME). The recommended dose is 2 milligrams (mg) aflibercept solution for injection into the eye equivalent to 50 microlitres. Treatment with aflibercept solution for injection is initiated with one injection into the eye per month for five consecutive doses, followed by one injection every two months into the eye without any requirement for monitoring between injections. After the first 12 months of treatment, the treatment interval may be extended based on visual and anatomic outcomes. The final decision of the European Commission is expected in the coming months.

“Early diagnosis of DME is critical,” said Dr. Joerg Moeller, Member of the Bayer HealthCare Executive Committee and Head of Global Development. “If DME is not treated rigorously, there is a high risk of DME leading to blindness. About half of the patients lose more than two lines of vision within two years of diagnosis without treatment, which can impact their ability to perform important daily activities such as working and driving.”

About the Phase 3 DME Program

The Phase 3 DME program consists of three double-masked trials: VIVID-DME, VISTA-DME, and VIVID-EAST-DME, and one open label single arm safety trial in Japanese patients (VIVID-Japan). All three double masked studies have three treatment arms, where patients are randomized to receive either aflibercept solution for injection 2 mg monthly, aflibercept solution for injection 2 mg every two months (after 5 initial monthly

injections), or the comparator treatment of laser photocoagulation. The primary endpoint of these three studies is the mean change in best-corrected visual acuity from baseline, as measured on the Early Treatment Diabetic Retinopathy Scale (ETDRS) eye chart, a standardized eye chart used in research to measure visual acuity, at Week 52. The VIVID-DME, VISTA-DME and VIVID-EAST-DME studies are ongoing.

The submission is based on data from the positive Phase 3 VIVID-DME and VISTA-DME studies which showed aflibercept solution for injection into the eye 2 mg every other month achieved rapid and sustained visual acuity gains compared to treatment with laser photocoagulation.

In the VIVID-DME study, after Week 52, patients receiving aflibercept solution for injection 2 mg every other month (after 5 initial monthly injections) had a mean gain from baseline in best corrected visual acuity (BCVA) of +10.7 letters ($p<0.0001$). This is equivalent to a gain of more than two lines on the ETDRS-eye chart. Patients receiving laser photocoagulation had a mean change from baseline in BCVA of +1.2 letters. Additionally, thirty-three percent (33.3 %) of patients receiving aflibercept solution for injection 2 mg every other month achieved an increase of ≥ 15 letters, a gain of three lines from baseline as one key secondary endpoint compared to the laser treatment group with only nine percent (9.1%) ($p<0.0001$) achieving a similar gain.

In the VISTA-DME study, after Week 52, 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 ($p<0.0001$), compared to patients receiving laser photocoagulation who had a mean change from baseline in BCVA of +0.2 letters. Additionally, as reflected by one of the secondary endpoints, thirty-one percent (31.1 %) of patients receiving aflibercept solution for injection 2 mg every other month achieved an increase of ≥ 15 letters from baseline compared to the laser treatment group with close to eight percent (7.8%) ($p<0.0001$) achieving a similar gain.

Further secondary endpoints in the VIVD-DME and VISTA-DME studies included the change from baseline in central retinal thickness, diabetic retinopathy severity score and vision related quality of life.

In both studies, aflibercept solution for injection was generally well tolerated with a similar overall incidence of adverse events (AEs), ocular serious AEs, and non-ocular serious AEs across the treatment groups and the laser control group. Arterial thromboembolic

events as defined by the Anti-Platelet Trialists' Collaboration (non-fatal stroke, non-fatal myocardial infarction, and vascular death) also occurred at similar rates across treatment groups and the laser control group. The most frequent ocular treatment emergent AEs (TEAEs) observed in the VIVID-DME and VISTA-DME studies included conjunctival hemorrhage, eye pain, and vitreous floaters. The most frequent non-ocular TEAEs included hypertension and nasopharyngitis, which occurred with similar frequency in the treatment groups and the laser control group.

The second year data from the VISTA-DME study show the improvement in visual acuity was maintained on extended treatment interval with injections every other month.

Aflibercept solution for injection into the eye has been approved under the brand name EYLEA® in many countries for the treatment of patients with neovascular age-related macular degeneration (wet AMD) and for the treatment of visual impairment due to macular edema secondary to central retinal vein occlusion (CRVO). Regulatory submissions have been made in Japan, Asia Pacific, Latin America and the U.S. for the treatment of Diabetic Macular Edema. In Japan, EYLEA has been additionally submitted for approval to regulators for the treatment of choroidal neovascularization secondary to pathologic myopia (mCNV). Furthermore a regulatory submission has been made in Europe and the U.S. for EYLEA for the treatment of visual impairment due to macular edema following 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 percentage of net sales.

About Diabetic Macular Edema (DME)
DME is a common complication of Diabetic Retinopathy, 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.

DME is the most frequent cause of blindness in young and mid-aged adults in most developed countries. The treatable population for DME globally is estimated at about 6.2 million people. The incidence of diabetes has been steadily climbing and it is projected

that up to seven percent of all patients with diabetes will develop DME during their lifetime.

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.

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 commercializes 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.

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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