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# Investor News

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Aflibercept solution for injection into the eye:

## Two-Year Results From Phase 3 Trial Show Sustained Improvement in Vision for People with Diabetic Macular Edema

**Leverkusen, Germany, July 18, 2014** – Bayer HealthCare today announced that in the Phase 3 VIVID-DME trial of aflibercept solution for injection into the eye for the treatment of vision impairment due to diabetic macular edema (DME), aflibercept solution for injection 2 milligrams (mg), in both treatment groups (dosed monthly or every two months), showed a sustained improvement from baseline in best corrected visual acuity (BCVA) at week 100, compared to laser photocoagulation.

“Giving people whose eyesight has been affected by diabetes the opportunity to maintain vision as good as possible each and every day is critical so they can continue performing their daily activities such as driving and working,” said Dr. Joerg Moeller, Member of the Bayer HealthCare Executive Committee and Head of Global Development. “We are encouraged by these data, along with the previously reported two-year data from the similarly designed VISTA-DME study. If approved, we hope aflibercept solution for injection may offer people affected by diabetic vision loss a new option to improve and sustain their vision.”

Patients in the VIVID-DME trial were randomized to receive either aflibercept solution for injection into the eye every month (n=136), aflibercept solution for injection every two months (after an initial injection every month for five consecutive doses) (n=135), or the comparator treatment of laser photocoagulation (n=132). After two years, patients receiving aflibercept solution for injection every month had a mean gain from baseline in BCVA of 11.4 letters (10.5 letters at 52 weeks; $p< 0.0001$). This is equivalent to a gain of more than two lines on the ETDRS-eye chart, a standard chart for measuring vision. Patients receiving aflibercept solution for injection every two months had a mean gain from baseline in BCVA of 9.4 letters (10.7 letters at 52 weeks; $p<0.0001$). Patients in the laser photocoagulation treatment group had a mean change from baseline in BCVA of 0.7

letters (1.2 letters at 52 weeks; p < 0.0001 for each of the aflibercept solution for injection arms vs. laser). Additionally, one third of patients (31.1%) receiving aflibercept solution for injection 2 mg every two months achieved an increase of ≥15 letters, a gain of three lines from baseline as one of the endpoints compared to the laser treatment group with only twelve percent (12.1%; p<0.0001) achieving a similar gain.

In this trial, 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 aflibercept solution for injection into the eye treatment groups and the laser treatment group. AEs were typical of those seen in other studies in patients with diabetes receiving intravitreal anti-VEGF therapy. The most frequent ocular AEs in the aflibercept solution for injection groups observed included conjunctival hemorrhage, cataract, and intraocular pressure increased. The most frequent non-ocular AEs in these groups included nasopharyngitis, hypertension, glycosylated haemoglobin increased. Arterial thromboembolic events as defined by the ´Anti-Platelet Trialists' Collaboration (non-fatal stroke, non-fatal myocardial infarction, and vascular death) were similar across the treatment groups and the laser group with events occurring in 8 out of 136 patients (5.9%) in the aflibercept solution for injection monthly group, 5 out of 135 patients (3.7%) in the aflibercept solution for injection every two months group, and 3 out of 133 patients (2.3%) in the laser group.

Full two-year data from the VIVID-DME trial will be presented at upcoming medical conferences. Both the VIVID-DME and the VISTA-DME trials will continue as planned up to 148 weeks.

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 Europe, Japan, Asia Pacific, Latin America and the U.S., for the treatment of DME. In Japan, EYLEA has been additionally submitted for approval to regulators for the treatment of choroidal neovascularization secondary to pathologic myopia (myopic CNV). 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 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 tool used in research to measure visual acuity, at 52 weeks. The VIVID-DME, VISTA-DME and VIVID-EAST-DME studies are ongoing.

**About Diabetic Macular Edema (DME)**

Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR) are common microvascular complications in people with diabetes. Diabetic Retinopathy 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.

DME is the most frequent cause of blindness in young and mid-aged adults. 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 people 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 into the eye 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 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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