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EYLEA® (AFLIBERCEPT) INJECTION RECEIVES FDA APPROVAL FOR THE TREATMENT OF DIABETIC MACULAR EDEMA (DME)

TARRYTOWN, N.Y., July 29, 2014 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today announced that the U.S. Food and Drug Administration (FDA) has approved EYLEA® (aflibercept) Injection for the treatment of Diabetic Macular Edema (DME). The recommended dosage of EYLEA in patients with DME is 2 milligrams (mg) every two months (8 weeks) after five initial monthly injections. Although EYLEA may be dosed as frequently as 2 mg every 4 weeks, additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks.

"Diabetic macular edema is a leading cause of vision loss among working-age adults in the U.S., and we are pleased to be able to offer a new treatment option to these patients," said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "Our clinical studies have demonstrated that treatment with EYLEA can help improve and maintain vision with every 8 week dosing after 5 initial monthly doses. EYLEA is the first VEGF inhibitor approved for dosing on a less than monthly basis for the treatment of DME."

The approval of EYLEA in DME was based on the one-year data from the Phase 3 VISTA-DME and VIVID-DME studies of 862 patients, which compared EYLEA 2 mg given monthly, EYLEA 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) chart for the monthly and every two month EYLEA groups, were statistically significantly improved compared to the control group and were similar to each other. Across both trials, patients in both EYLEA dosing groups gained, on average, the ability to read approximately two additional lines on an eye chart compared with almost no change in the control group.

In these trials, EYLEA had a similar overall incidence of adverse events (AEs), ocular serious AEs, and non-ocular serious AEs across treatment groups and the 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 control group. The most frequent ocular treatment emergent AEs (TEAEs) observed in the VISTA-DME and VIVID-DME trials included conjunctival hemorrhage, eye pain, cataract, and vitreous floaters. The most common non-ocular TEAEs included hypertension and nasopharyngitis, which occurred with similar frequency in the treatment groups and the control group.

EYLEA is available as a single, 2-mg strength intravitreal injection for all approved indications. EYLEA was approved in the United States for the treatment of neovascular (wet) Age-related Macular Degeneration (AMD) in 2011, and for the treatment of Macular Edema following Central Retinal Vein Occlusion (CRVO) in 2012. EYLEA has also been approved in the EU and other countries for use in wet AMD and Macular Edema following CRVO. In Europe, the Committee for Medicinal Products for Human Use has given a positive opinion recommending approval for EYLEA in the treatment of DME. Regulatory submissions have also been made in Japan, Asia Pacific, and Latin America 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). A regulatory submission has been made in the U.S. and EU for EYLEA for the treatment of Macular Edema following Branch Retinal Vein Occlusion (BRVO).

Phase 3 Study Details

In the Phase 3 VISTA-DME and VIVID-DME trials, EYLEA® (aflibercept) Injection 2 mg dosed monthly and EYLEA 2 mg dosed every two months after 5 initial monthly doses achieved statistically significant improvements in the primary endpoint of mean change in BCVA at one year and the secondary endpoint of proportion of patients who gained at least 15 letters in BCVA versus baseline compared to control.

In the VISTA-DME trial, patients receiving EYLEA 2 mg monthly had a mean change from baseline in BCVA of 12.5 letters (*P less than 0.01 compared to control*), patients receiving EYLEA 2 mg every two months (after 5 initial monthly injections) had a mean change from baseline in BCVA of 10.7 letters (*P less than 0.01 compared to control*), and

percent in the EYLEA 2 mg every month group (*P less than 0.01 compared to control*), 31.1 percent in the EYLEA 2 mg every 2 months group (after 5 initial monthly injections) (*P less than 0.01 compared to control*), and 7.8 percent in the control group.

In the VIVID-DME trial, patients receiving EYLEA 2 mg monthly had a mean change from baseline in BCVA of 10.5 letters (*P less than 0.01 compared to control*), patients receiving EYLEA 2 mg every two months (after 5 initial monthly injections) had a mean change from baseline in BCVA of 10.7 letters (*P less than 0.01 compared to control*), and patients receiving control had a mean change from baseline in BCVA of 1.2 letters. In the VIVID-DME trial, the percentage of patients who gained at least 15 letters in BCVA from baseline, or three lines of vision, was 32.4 percent in the EYLEA 2 mg every month group (*P less than 0.01 compared to control*), 33.3 percent in the EYLEA 2 mg every 2 months group (after 5 initial monthly injections) (*P less than 0.01 compared to control*), and 9.1 percent in the control group.

In these trials, EYLEA had a similar overall incidence of adverse events (AEs), ocular serious AEs, and non-ocular serious AEs across treatment groups and the 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 control group. The most frequent ocular treatment emergent AEs (TEAEs) observed in the VISTA-DME and VIVID-DME trials at one year included conjunctival hemorrhage, eye pain, cataract, and vitreous floaters. The most common non-ocular TEAEs at one year included hypertension and nasopharyngitis, which occurred with similar frequency in the treatment groups and the control group.

The VISTA-DME and VIVID-DME studies will continue as planned for a total of three years.

About Diabetic Macular Edema (DME)
Diabetic Macular Edema (DME) or "swelling of the macula" is a common complication in the eyes of patients with diabetes. It is the most frequent cause of vision loss in patients with diabetes and eventually can lead to blindness.[1,2] It is estimated that of the 29.1 million American adults living with diabetes, 1.5 million have been diagnosed with DME, and approximately another million cases are undiagnosed.[3,4,5]

DME occurs when blood vessels in the retina are damaged by chronic high blood sugar levels caused by diabetes. This allows fluid from blood vessels to leak into the retina, causing macular swelling. Fluid in the macula can cause severe vision loss or blindness. The macula is the part of the retina responsible for central, fine vision.

Vascular endothelial growth factor (VEGF), a naturally occurring family of growth factors in the body, appears to play a critical role in the development of DME. Increased VEGF production contributes to the vascular disruptions and leakage that characterize DME, as well as the formation of new blood vessels (a process known as angiogenesis).

About EYLEA® (aflibercept) Injection for Intravitreal Injection
EYLEA is a vascular endothelial growth factor (VEGF) inhibitor formulated as an injection for the eye. EYLEA is designed to block the growth of new blood vessels and decrease the ability of fluid to pass through blood vessels (vascular permeability) in the eye by blocking VEGF-A and placental growth factor (PlGF), two growth factors involved in angiogenesis. EYLEA helps prevent VEGF-A and PlGF from interacting with their natural VEGF receptors as shown in preclinical studies.

IMPORTANT PRESCRIBING INFORMATION FOR EYLEA® (aflibercept) INJECTION

EYLEA® (aflibercept) Injection is a prescription medicine approved for the treatment of patients with: Wet AMD: The recommended dose for EYLEA is 2 mg administered by injection in the eye every 2 months (8 weeks) following 3 initial monthly (4 weeks) injections. EYLEA may be dosed once per month, but additional benefit was not seen with this dosing plan.

Macular Edema following CRVO: The recommended dose for EYLEA is 2 mg administered by injection in the eye monthly (every 4 weeks).

Diabetic Macular Edema: The recommended dose for EYLEA is 2 mg administered by injection in the eye every 2 months (8 weeks) following 5 initial monthly (4 weeks) injections. EYLEA may be dosed once per month, but additional benefit was not seen with this dosing plan.

IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION

EYLEA® (aflibercept) Injection is a prescription medication administered by injection into the eye. You should not use EYLEA if you have an infection in or around the eye, eye pain or redness, or known allergies to any of the ingredients in EYLEA, including aflibercept. As with all medications, EYLEA can cause side effects.

Injection into the eye can result in an infection in the eye and retinal detachment. Inflammation in the eye has been reported with the use of EYLEA.

In some patients, injections with EYLEA may trigger a temporary increase in eye pressure within 1 hour of the injection. Sustained increases in eye pressure have been reported with repeated injections and your doctor may

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There is a potential risk of serious and sometimes fatal side effects related to blood clots, leading to heart attack or stroke in patients receiving EYLEA.

The most common side effects reported in patients receiving EYLEA are increased redness in the eye, eye pain, cataract, moving spots in the field of vision, increased pressure in the eye and vitreous (gel-like substance) detachment.

Serious side effects related to the injection procedure are rare but can occur including infection inside the eye, retinal detachment, cataract, increased pressure in the eye, and vitreous detachment. It is important that you contact your doctor right away if you think you might be experiencing any side effects.

EYLEA is for prescription use only. For additional safety information, please talk to your doctor and see the full Prescribing Information for EYLEA.

Please see the full U.S. Prescribing Information for EYLEA at www.EYLEA.com.

The product information is intended only for residents of the United States. The product discussed herein may have different labeling in different countries.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

About the EYLEA® (aflibercept) Injection Global Collaboration
Bayer HealthCare and Regeneron are collaborating on the global development of EYLEA. Regeneron maintains exclusive rights to EYLEA in the United States. Bayer HealthCare has 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 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.

Regeneron Forward-Looking Statements
This news release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron, and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the nature, timing, and possible success and therapeutic applications of Regeneron's products, product candidates, and research and clinical programs now underway or planned, including without limitation EYLEA® (aflibercept) Injection; unforeseen safety issues resulting from the administration of products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's product candidates in clinical trials, such as the EYLEA® (aflibercept) Injection VIVID-DME and VISTA-DME studies; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products, such as EYLEA® (aflibercept) Injection in the treatment of choroidal neovascularization secondary to pathologic myopia and macular edema following Branch Retinal Vein Occlusion; ongoing regulatory obligations and oversight impacting Regeneron's research and clinical programs and business, including those relating to patient privacy; determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize Regeneron's products and product candidates; competing drugs and product candidates that may be superior to Regeneron's products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's products and product candidates; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; coverage and reimbursement determinations by third-party payers, including Medicare and Medicaid; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its sales or other financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license or collaboration agreement, including Regeneron's agreements with Sanofi and Bayer HealthCare LLC, to be cancelled or terminated without any further product success; and risks associated with intellectual property of other parties and pending or future litigation relating thereto. A more complete description of these and other material risks can be found in Regeneron's filings with the United States Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2013 and its Form 10-Q for the quarter ended March 31, 2014. The reader is cautioned not to rely on any forward-looking statements made by Regeneron. Regeneron does not undertake any obligation to update publicly any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

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