EYLEA® (aflibercept) Injection Receives FDA Breakthrough Therapy Designation for Diabetic Retinopathy in Patients with Diabetic Macular Edema

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TARRYTOWN, N.Y., Sept. 16, 2014 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today announced that the U.S. Food and Drug Administration (FDA) has granted EYLEA® (aflibercept) Injection Breakthrough Therapy designation for the treatment of diabetic retinopathy in patients with diabetic macular edema (DME). The designation is based on positive results in two Phase 3 trials (VIVID-DME and VISTA-DME), in which EYLEA demonstrated a statistically significant improvement in a pre-specified measure of diabetic retinopathy in patients with DME after two years of treatment.

"Millions of people in the U.S. are living with diabetic eye diseases that can cause vision loss and even blindness," said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "There are no FDA-approved medicines for diabetic retinopathy and we look forward to working closely with the FDA to potentially bring EYLEA to these patients as soon as possible. We plan to submit a supplemental Biologics License Application (sBLA) in the U.S. for diabetic retinoapthy in patients with DME later this year."

In the Phase 3 VIVID-DME trial in diabetic retinopathy patients with DME, 29 percent of evaluable patients in the 2Q4 group (monthly) and 33 percent of evaluable patients in the 2Q8 group (every two months, after 5 initial monthly injections) treated with EYLEA experienced at least a 2-step improvement on the diabetic retinopathy severity scale (DRSS), a grading system measuring the degree of retinopathy, compared to 8 percent of patients in the laser control group (p less than 0.001). In the Phase 3 VISTA-DME trial in diabetic retinopathy patients with DME, 40 percent of evaluable patients in both the 2Q4 and 2Q8 groups treated with EYLEA experienced at least a 2-step improvement on the DRSS compared to 17 percent of patients in the laser control group (p less than 0.0001). The most frequent ocular adverse events (AEs) observed in the VIVID-DME trial were conjunctival hemorrhage, cataract, and increased intraocular pressure. The most frequent ocular AEs observed in the VISTA-DME trial were conjunctival hemorrhage, eye pain, and vitreous floaters. The two-year results from these trials on the primary endpoint of best-corrected visual acuity (BCVA) and overall safety have been previously announced and are available here.

The Breakthrough Therapy designation was created by the FDA to expedite the development and review of drugs for serious or life-threatening conditions. Drugs qualifying for this designation must show credible evidence of a substantial improvement on a clinically significant endpoint over available therapies, or over placebo if there is no available therapy. The designation includes all of the fast track program features, as well as more intensive FDA guidance and discussion. The Breakthrough Therapy designation is distinct from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met.

EYLEA is approved in the United States, European Union (EU) and other countries for the treatment of wet age-related macular degeneration (AMD), macular edema following central retinal vein occlusion (CRVO), and DME. Regulatory submissions have been made for EYLEA in the U.S. and EU for macular edema following branch retinal vein occlusion (BRVO).

About Diabetic Retinopathy and Diabetic Macular Edema (DME)
Diabetic retinopathy is a common complication of diabetes, causing damage to the retina, which may lead to poor vision and vision loss. Over time, patients with diabetic retinopathy are at risk of experiencing vision-threatening events. These include DME, which refers to the swelling of the macula (the part of the retina responsible for central, fine vision) and progression to proliferative diabetic retinopathy, which often results in profound visual loss due to associated complications including vitreous hemorrhage and/or tractional retinal detachment. DME 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, 7.7 million have diabetic retinopathy, 1.5 million have been diagnosed with DME and approximately another million cases of DME are undiagnosed.[3,4,5] Diabetic retinopathy and DME occur when blood vessels in the retina are damaged by chronic high blood sugar levels caused by diabetes.

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.

About Diabetic Retinopathy Severity Scale (DRSS)
Derived from The Early Treatment Diabetic Retinopathy Study (ETDRS), the diabetic retinopathy severity scale (DRSS) is a systematic grading system developed to predict the risk of progression from non-proliferative diabetic retinopathy (NPDR) to proliferative diabetic retinopathy (PDR). The DRSS characterizes retinopathy based on assessment of abnormalities in seven defined fields of fundus photographs. The scale divides diabetic retinopathy into levels ranging from absent to severe proliferative diabetic retinopathy. This scale has become the gold standard for grading degrees of retinopathy in clinical studies.

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 monitor this after each injection.

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 diabetic retinopathy in patients with diabetic macular edema; 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 June 30, 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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SOURCE Regeneron Pharmaceuticals, Inc.