EYLEA® (aflibercept) Injection Receives FDA Approval for the Treatment of Diabetic Retinopathy in Patients with Diabetic Macular Edema (DME)

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TARRYTOWN, N.Y., March 25, 2015 /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 retinopathy in patients with diabetic macular edema (DME). In 2014, the FDA granted EYLEA Breakthrough Therapy designation and Priority Review for the treatment of diabetic retinopathy in patients with DME.

"Diabetic retinopathy coupled with DME is a serious complication of diabetes that can threaten the vision of many working-age adults," said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "In addition to improving visual acuity in people with DME, EYLEA also improves these patients' retinal vessel damage, or retinopathy. EYLEA is the only treatment option for diabetic retinopathy in patients with DME that is approved for less than monthly dosing after an initial monthly dosing period."

The recommended dosage of EYLEA in patients with diabetic retinopathy in 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.

EYLEA is available as a single, 2 milligram (mg) strength intravitreal injection for all approved indications. EYLEA was previously approved in the U.S. for the treatment of wet age-related macular degeneration (AMD), macular edema following retinal vein occlusion (RVO), and diabetic macular edema (DME).

About the VISTA-DME and VIVID-DME Trials
The approval of EYLEA for the treatment of diabetic retinopathy in DME was based on two year data from the Phase 3 VISTA-DME and VIVID-DME studies of 862 patients, which compared EYLEA 2 mg monthly, EYLEA 2 mg every two months (after five initial monthly injections), or macular laser photocoagulation (at baseline and then as needed). In these studies, on the primary endpoint of mean change in Best Corrected Visual Acuity (BCVA) at one year, patients treated with EYLEA monthly or every two months showed statistically significant improvements compared to the control group. Patients in both EYLEA 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.

A pre-specified secondary endpoint in the studies at year 2 evaluated diabetic retinopathy severity based on an established grading scale measuring retinal damage. In the VISTA-DME trial, 38 percent of patients receiving EYLEA monthly or every two months (after 5 initial monthly injections) achieved a 2-step or better improvement on the diabetic retinopathy severity scale (DRSS), compared to 16 percent of patients receiving control. In the VIVID-DME trial, approximately 30 percent of patients receiving EYLEA monthly or every two months (after 5 initial monthly injections) achieved a 2-step or better improvement on the DRSS, compared to 8 percent of patients receiving control.

In these trials at year 2, 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.

About Diabetic Retinopathy with 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 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 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]

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 diabetic retinopathy and, subsequently, DME. Increased VEGF production contributes to the vascular disruptions associated with diabetic retinopathy and the subsequent leakage that characterizes 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 Age-related Macular Degeneration (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 Retinal Vein Occlusion (RVO): The recommended dose for EYLEA is 2 mg administered by injection in the eye monthly (every 4 weeks).

Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR) in patients with DME: 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.

Serious side effects related to the injection procedure are rare but can occur including infection inside the eye and retinal detachment.

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.

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.

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.

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 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 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 press release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("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; 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; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products; ongoing regulatory obligations and oversight impacting Regeneron's marketed products (such as EYLEA® (aflibercept) Injection), 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 and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on the 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 U.S. Securities and Exchange Commission, including its Form 10-K for the fiscal year ended December 31, 2014. Any forward-looking statements are made based on management's current beliefs and judgment, and 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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