Regeneron Announces FDA Approval of EYLEA® (aflibercept) Injection For Macular Edema Following Central Retinal Vein Occlusion

September 21, 2012

TARRYTOWN, N.Y., Sept. 21, 2012 /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 Macular Edema following Central Retinal Vein Occlusion (CRVO). The recommended dose for EYLEA is 2 milligrams (mg) every 4 weeks (monthly).

"This second U.S. approval for EYLEA provides physicians and patients with a new treatment option for the treatment of macular edema following CRVO," stated George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "Based upon the pivotal Phase 3 study results, EYLEA has been shown to significantly improve visual outcomes in a disease characterized by high VEGF levels. We thank the patients and clinical investigators who participated in our clinical studies, the FDA, and the Regeneron employees who helped make this day possible."

The approval of EYLEA for Macular Edema following CRVO was based on data from the Phase 3 COPERNICUS and GALILEO studies. In both studies, the primary efficacy endpoint was the proportion of patients who gained at least 15 letters of Best Corrected Visual Acuity (BCVA) at 24 weeks compared to baseline as measured by ETDRS. Results for the EYLEA 2 mg monthly group were superior to those for the sham control group for the primary endpoint.

EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

Results from week 24 through 52 of the COPERNICUS and GALILEO studies have not yet been reviewed by the FDA.

About EYLEA® (aflibercept) Injection For Intravitreal Injection
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. However, in certain diseases, such as wet age-related macular degeneration, it is also associated with the growth of abnormal new blood vessels in the eye, which exhibit abnormal increased permeability that leads to edema. Scarring and loss of fine-resolution central vision often results. In Central Retinal Vein Occlusion (CRVO), a blockage occurs in the main blood vessel that transports deoxygenated blood away from the retina. VEGF levels are elevated in response contributing to macular edema.

EYLEA 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. EYLEA acts as a soluble decoy receptor that binds VEGF-A and placental growth factor (PlGF) and thereby can inhibit the binding and activation of these cognate VEGF receptors. EYLEA is specially purified and contains iso-osmotic buffer concentrations, allowing for injection into the eye.

About the Phase 3 Program with EYLEA® (aflibercept) Injection in Macular Edema Following CRVO

The safety and efficacy of EYLEA in the treatment of Macular Edema following CRVO were assessed in two randomized, multi-center, double-masked, sham-controlled studies: COPERNICUS (Controlled Phase 3 Evaluation of Repeated intravitreal administration of VEGF Trap-Eye In Central retinal vein occlusion: Utility and Safety) and GALILEO (General Assessment Limiting Infiltration of Exudates in central retinal vein Occlusion with EYLEA).

A total of 358 patients were treated and evaluable for efficacy (217 with EYLEA) in COPERNICUS and GALILEO. In both studies, patients were randomly assigned in a 3:2 ratio to either 2 mg EYLEA administered every 4 weeks (Q4), or sham injections (control group) administered every 4 weeks for a total of 6 injections. After 6 monthly injections, patients continued to receive EYLEA treatment during weeks 24 to 52 only if they met pre-specified retreatment criteria (PRN), except for patients in the sham control group in the GALILEO study who continued to receive sham injections through week 52. Patients ranged in age from 22 to 89 years with a mean of 64 years.

In the COPERNICUS study, after six months, 56% of patients receiving EYLEA 2 mg monthly gained at least 15 letters of Best Corrected Visual Acuity (BCVA) from baseline, as measured by ETDRS, compared to 12% of patients receiving sham injections ($p < 0.01$), the primary endpoint of the study. Patients receiving EYLEA 2 mg monthly gained, on average, 17.3 letters of vision compared to a mean loss of 4.0 letters with sham control injections ($p < 0.01$), a secondary endpoint.

In the GALILEO study, after six months, 60% of patients receiving EYLEA 2 mg monthly for the first 6 months, gained at least 15 letters of BCVA from baseline, compared to 22% of patients receiving sham injections ($p < 0.01$) during this time, the primary endpoint of the study. Patients receiving EYLEA 2 mg monthly gained, on average, 18.0 letters of vision compared to a mean gain of 3.3 letters with sham control injections ($p < 0.01$), a secondary endpoint.

Results from week 24 through 52 of the COPERNICUS and GALILEO studies have not yet been reviewed by the FDA.

IMPORTANT PRESCRIBING INFORMATION FOR EYLEA® (aflibercept) INJECTION
In the United States, EYLEA® (aflibercept) Injection is indicated for the treatment of patients with neovascular (Wet) Age-related Macular Degeneration (AMD). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg once every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks.

In the United States, EYLEA is indicated for the treatment of patients with Macular Edema following Central Retinal Vein Occlusion (CRVO). The recommended dose for EYLEA is 2 mg administered by intravitreal injection every 4 weeks (monthly).

IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION

EYLEA® (aflibercept) Injection is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported during the post approval use of EYLEA.

Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.

There is a potential risk of arterial thromboembolic events (ATEs) following use of intravitreal VEGF inhibitors, including EYLEA, defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of ATEs in the VIEW 1 and VIEW 2 wet AMD studies in patients treated with EYLEA was 1.8% during the first year. The incidence of ATEs in the COPERNICUS and GALILEO CRVO studies was 0% in patients treated with EYLEA compared with 1.4% in patients receiving sham control during the first six months.

The most common adverse reactions (5% or more) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and increased intraocular pressure.

Serious adverse reactions related to the injection procedure have occurred in &< 0.1% of intravitreal injections with EYLEA including endophthalmitis, traumatic cataract, increased intraocular pressure, and vitreous detachment.

Please see the full Prescribing Information at www.EYLEA.com.

About the EYLEA® (aflibercept) Injection Global Collaboration

Regeneron is collaborating with Bayer HealthCare on the global development of EYLEA. In June 2011, Bayer HealthCare submitted an application for marketing authorization in Europe for neovascular (wet) age-related macular degeneration (wet AMD). Bayer Healthcare's Japanese subsidiary, Bayer Yakuhin, has submitted an application for marketing authorization to the Ministry of Health, Labor and Welfare (MHLW) for EYLEA for the treatment of wet AMD. EYLEA has received approval from the Australian Therapeutic Goods Administration (TGA) for the treatment of patients with wet AMD. The drug has also received marketing approval in Colombia for wet AMD.

Bayer HealthCare will market EYLEA outside the United States, where the companies will share equally the profits from any future sales of EYLEA. Regeneron maintains exclusive rights to EYLEA in the United States.

About Central Retinal Vein Occlusion

Over 100,000 people in the United States are estimated to suffer from CRVO. CRVO is caused by obstruction of the central retinal vein that leads to a back up of blood and fluid in the retina. This causes retinal damage and loss of vision. Release of vascular endothelial growth factor (VEGF) contributes to increased vascular permeability in the eye and macular edema. It is believed that anti-VEGF treatment may help decrease vascular permeability and edema in the retina in patients with CRVO.

About Regeneron Pharmaceuticals

Regeneron is a fully integrated biopharmaceutical company that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. Regeneron markets three products in the United States, EYLEA® (aflibercept) Injection, ZALTRAP® (ziv-aflibercept) Injection for Intravenous Infusion, and ARCALYST® (rilonacept) Injection for Subcutaneous Use; ZALTRAP is co-commercialized with Sanofi. Phase 3 studies are in progress with EYLEA in two additional indications and with product candidates sarilumab and REGN727. Regeneron has active research and development programs in many disease areas, including ophthalmology, inflammation, cancer, and hypercholesterolemia. Additional information and recent news releases are available on the Regeneron web site at www.regeneron.com.

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. 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), unforeseen safety issues resulting from the administration of products and product candidates in patients, the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates, 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 drug candidates, competing drugs that may be superior to Regeneron's products and drug candidates, uncertainty of market acceptance of Regeneron's products and drug candidates, unanticipated expenses, the costs of developing, producing, and selling products, the potential for any license or collaboration agreement, including Regeneron's agreements with Sanofi and Bayer HealthCare, to be canceled or terminated, and risks associated with third party intellectual property 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, 2011 and its Form 10-Q for the quarter ended June 30, 2012. Regeneron does not undertake any obligation to update publicly any forward-looking statement, whether as a result of new information, future events, or otherwise, unless required by law.

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