# Regeneron Reports Positive Phase 3 Data for EYLEA® (aflibercept) Injection in Macular Edema Following Branch Retinal Vein Occlusion

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TARRYTOWN, N.Y., Oct. 21, 2013 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today announced positive topline results for EYLEA® (aflibercept) Injection from the Phase 3 VIBRANT study in patients with Macular Edema following Branch Retinal Vein Occlusion (BRVO). In this trial, 53% of patients who received EYLEA 2 milligram (mg) every four weeks gained at least 15 letters in vision from baseline at week 24, the primary endpoint of the study, compared to 27% of patients who received laser, a standard-of-care treatment (p &< 0.001). Patients who received EYLEA 2 mg every four weeks achieved a 17.0 letter mean improvement over baseline in best corrected visual acuity (BCVA) compared to a 6.9 letter mean improvement in patients who received laser (p &< 0.0001), a key secondary endpoint. VIBRANT is the first Phase 3 trial in this indication in which an anti-VEGF agent was directly compared to an active comparator.

The incidence of serious adverse events (SAE) was 9.9% in the EYLEA group and 9.8% in the laser group. One death and one Anti-Platelet Trialists' Collaboration (APTC) defined event (non-fatal stroke) occurred during the trial, both in patients in the laser group. The most common ocular adverse events in the EYLEA treated patients were conjunctival hemorrhage and eye pain. There were no cases of intraocular inflammation. There was one ocular SAE in a patient in the EYLEA group, which was a traumatic cataract.

"These positive data in patients with macular edema following BRVO further support the efficacy of EYLEA in a broad spectrum of retinal diseases," stated George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "If approved, we hope to be able to offer physicians and patients a new treatment option for addressing macular edema associated with this severe and potentially blinding retinal disorder."

"VIBRANT represents the eighth positive trial from the EYLEA Phase 3 program, which has enrolled over 3,800 patients from around the world and highlights our commitment to retinal diseases," said Robert Vitti, M.D., Vice President, Clinical Sciences, Ophthalmology, Regeneron Pharmaceuticals. "We want to thank all the investigators and patients involved in this study. We are proud of the effort consistently put forth by the EYLEA development team."

Detailed results from this study will be presented at an upcoming medical conference. Regeneron intends to submit a regulatory application for marketing approval for macular edema following BRVO in the U.S. within the next several months.

EYLEA was approved in the United States for the treatment of neovascular (wet) Age-related Macular Degeneration (AMD) in November 2011 and for Macular Edema following Central Retinal Vein Occlusion (CRVO) in September 2012. EYLEA has also been approved in Europe, Japan, Australia, and in many other countries for use in wet AMD and in Europe and other countries for Macular Edema following CRVO.

Bayer HealthCare and Regeneron 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 royalty on net sales.

**About the Phase 3 VIBRANT Study**

The Phase 3 VIBRANT trial was a double-masked, randomized, active-controlled study of 183 patients with Macular Edema following Branch Retinal Vein Occlusion. Patients received either intravitreal EYLEA 2 mg every four weeks or laser treatment, through week 24. The primary objective of the study was to evaluate the efficacy and safety of EYLEA in improving best-corrected visual acuity compared to laser treatment at week 24. The study is ongoing through week 52.

**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. 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. In Branch Retinal Vein Occlusion (BRVO), a blockage occurs in one of the branching retinal veins that drain blood from the retina. The blockage leads to a backup of blood and fluid collection (macular edema) that can cause impairment of vision.

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 their cognate VEGF receptors.

**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.

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 with the 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) noted in the U.S. prescribing information for the approved indications of 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 U.S. Prescribing Information for EYLEA at www.EYLEA.com**

**About the EYLEA® (aflibercept) Injection Global Collaboration**

Regeneron is collaborating with Bayer HealthCare on the global development of EYLEA. EYLEA is currently approved for the treatment of wet AMD in approximately 50 countries outside the U.S., including Japan and Australia and countries in the E.U.

Regeneron maintains exclusive rights to EYLEA in the United States.

**About Branch Retinal Vein Occlusion**

Retinal Vein Occlusion is the second most common retinal vascular disorder and is a significant cause of visual impairment. Of the two main types of retinal vein occlusion -- CRVO and BRVO -- the latter is more common. In Branch Retinal Vein Occlusion (BRVO), a blockage occurs in the blood vessels branching from the main vein draining the retina, resulting in the release of VEGF and consequent retinal edema.

**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 markets 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; 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 the application of EYLEA® (aflibercept) Injection in the treatment Macular Edema following Branch Retinal Vein Occlusion; ongoing regulatory obligations and oversight and 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, to be cancelled or terminated without any further product success; 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, 2012 and Form 10-Q for the quarter ended June 30, 2013. 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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