



## **Regeneron Announces FDA Acceptance of EYLEA® (afibercept) Injection Supplemental Biologics License Application for the Treatment of Macular Edema Following Branch Retinal Vein Occlusion**

February 24, 2014

TARRYTOWN, N.Y., Feb. 24, 2014 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced that the U.S. Food and Drug Administration (FDA) has accepted for standard review the Company's supplemental Biologics License Application (sBLA) for EYLEA® (afibercept) Injection for the treatment of Macular Edema following Branch Retinal Vein Occlusion (BRVO). Under the Prescription Drug User Fee Act (PDUFA), the goal for a standard review of an sBLA is ten months from submission, for a target action date of October 23, 2014.

"We are pleased that the FDA has accepted the sBLA for EYLEA for the treatment of macular edema following BRVO, an important cause of vision loss," said George D. Yancopoulos, M.D., Ph. D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "This is the fourth regulatory submission in the U.S. for EYLEA and, if approved, we hope it will provide a new treatment option for patients with macular edema following BRVO."

The EYLEA sBLA submission in this indication is based on the positive results from the Phase 3 VIBRANT trial, which 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 milligrams (mg) every four weeks or laser treatment for 24 weeks. 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.

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 the European Union (EU) and other countries for use in wet AMD and Macular Edema following CRVO. Regulatory submissions have also been made in the U.S. and the EU for EYLEA for the treatment of Diabetic Macular Edema.

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 percentage of net sales.

### **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 BRVO, a blockage occurs in the blood vessels branching from the main vein draining the retina, resulting in the release of vascular endothelial growth factor and consequent retinal edema.

### **About EYLEA® (afibercept) 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.

EYLEA, known in the scientific literature as VEGF Trap-Eye, 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 (PIGF) and thereby can inhibit the binding and activation of their cognate VEGF receptors.

### **IMPORTANT PRESCRIBING INFORMATION FOR EYLEA® (afibercept) INJECTION IN THE UNITED STATES**

EYLEA® (afibercept) 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® (afibercept) INJECTION**

EYLEA® (afibercept) Injection is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to afibercept 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](http://www.EYLEA.com)**

#### **About the EYLEA® (afibercept) 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 EU. EYLEA has also been approved by the European Commission and in Japan for the treatment of visual impairment due to Macular Edema secondary to CRVO.

Regeneron maintains exclusive rights to EYLEA in the United States.

#### **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](http://www.regeneron.com).

#### **About Bayer HealthCare**

The Bayer Group is a global enterprise with core competencies in the fields of health care, agriculture and high-tech materials. Bayer HealthCare, a subgroup of Bayer AG with annual sales of EUR 18.6 billion (2012), is one of the world's leading, innovative companies in the healthcare and medical products industry and is based in Leverkusen, Germany. The company combines the global activities of the Animal Health, Consumer Care, Medical Care and Pharmaceuticals divisions. Bayer HealthCare's aim is to discover, develop, manufacture and market products that will improve human and animal health worldwide. Bayer HealthCare has a global workforce of 55,300 employees (Dec 31, 2012) and is represented in more than 100 countries. More information at [www.healthcare.bayer.com](http://www.healthcare.bayer.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®(afibercept) 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® (afibercept) Injection in the treatment of Macular Edema following Branch Retinal Vein Occlusion and in the treatment of 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, 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, 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.*

Your Investor Relations Contact at Regeneron:

**Manisha Narasimhan, Ph.D. Tel. 914.847.5126**

E-Mail: [manisha.narasimhan@regeneron.com](mailto:manisha.narasimhan@regeneron.com)

Your Media Contact at Regeneron:

**Sandy Sexton, Tel. 914.847.3358**

E-Mail: [sandra.sexton@regeneron.com](mailto:sandra.sexton@regeneron.com)

SOURCE Regeneron Pharmaceuticals, Inc.

News Provided by Acquire Media