August 6, 2013

Regeneron and Bayer Report Positive One-Year Results from Two Phase 3 Trials of EYLEA® (aflibercept) Injection for the Treatment of Diabetic Macular Edema

U.S. and ex-U.S. regulatory submissions in diabetic macular edema expected in 2013; U.S. regulatory submission approximately one year earlier than previously planned

TARRYTOWN, N.Y., Aug. 6, 2013 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) and Bayer HealthCare today announced that in the Phase 3 VIVID-DME and VISTA-DME trials of EYLEA® (aflibercept) Injection for the treatment of diabetic macular edema (DME), EYLEA 2 milligrams (mg) dosed monthly and EYLEA 2 mg dosed every two months (after 5 initial monthly injections) achieved the primary endpoint of a significantly greater improvement in best-corrected visual acuity (BCVA) from baseline compared to laser photocoagulation at 52 weeks. Both EYLEA treatment arms demonstrated similar improvements in BCVA.

Based on discussions with the U.S. Food and Drug Administration (FDA), Regeneron now expects to submit an application for U.S. marketing approval for the treatment of DME in 2013, approximately one year ahead of the previously announced timeline. Bayer Healthcare plans to submit an application for marketing approval for the treatment of DME in Europe in 2013.

The VIVID-DME and VISTA-DME trials are similarly designed, randomized, double-masked, active control trials to evaluate the safety and efficacy of EYLEA in patients with DME. Patients in both trials were randomized to receive either EYLEA 2 milligrams (mg) monthly, EYLEA 2 mg every two months (after 5 initial monthly injections), or the comparator treatment of laser photocoagulation.

"We are pleased with these positive data in another potentially important indication for EYLEA," said George D. Yancopoulos, M.D., Ph. D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "Diabetes is a growing disease worldwide and DME is a major cause of vision loss in people with diabetic retinopathy. We hope to be able to offer a new treatment option for patients suffering from this potentially blinding retinal disease."

In the VIVID-DME trial, after one year patients receiving EYLEA 2 mg monthly had a mean change from baseline in BCVA of 10.5 letters ($p < 0.0001$ compared to laser) and patients receiving EYLEA 2 mg every other month (after 5 initial monthly injections) had a mean change from baseline in BCVA of 10.7 letters ($p < 0.0001$ compared to laser), compared to patients receiving laser photocoagulation who had a mean change from baseline in BCVA of 1.2 letters.

In the VISTA-DME trial, after one year patients receiving EYLEA 2 mg monthly had a mean change from baseline in best-corrected visual acuity (BCVA) of 12.5 letters ($p < 0.0001$ compared to laser) and patients receiving EYLEA 2 mg every other month (after 5 initial monthly injections) had a mean change from baseline in BCVA of 10.7 letters ($p < 0.0001$ compared to laser), compared to patients receiving laser photocoagulation who had a mean change from baseline in BCVA of 0.2 letters.

In these trials, EYLEA was generally well tolerated with a similar overall incidence of adverse events (AEs), ocular serious AEs, and non-ocular serious AEs across the treatment groups and the laser 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 the treatment groups and the laser control group. AEs were typical of those seen in other studies in patients with diabetes receiving intravitreal anti-VEGF therapy. The most frequent ocular treatment emergent AEs (TEAEs) observed in the VIVID-DME and VISTA-DME trials included conjunctival hemorrhage, eye pain, and vitreous floaters. The most frequent non-ocular TEAEs included hypertension and nasopharyngitis, which occurred with similar frequency in the treatment groups and the laser control group.

Full one-year data from the VIVID-DME and VISTA-DME trials will be presented at upcoming medical conferences. Both trials are planned to continue up to 148 weeks.

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 several other countries for use in wet AMD.

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.

Topline results from these trials will be discussed on the previously scheduled Regeneron quarterly earnings conference call at 8:30 AM EDT today.

About the EYLEA® (aflibercept) Injection Phase 3 DME Program
The Phase 3 DME program consists of three double-masked trials: VIVID-DME, VISTA-DME, and VIVID-EAST-DME (in Russia, China and other Asian countries), and one open-label, single arm safety trial in Japanese patients (VIVID-Japan). All three double-masked studies have three treatment arms, where patients are randomized to receive either EYLEA 2 mg monthly, EYLEA 2 mg every two months (after 5 initial monthly injections), or the comparator treatment of laser photocoagulation. The primary endpoint of all three studies is the mean change in best-corrected visual acuity from baseline, as measured on the Early Treatment Diabetic Retinopathy Scale (ETDRS) eye chart, a standard chart used in research to measure visual acuity. The VIVID-DME, VISTA-DME, VIVID-EAST-DME, and VIVID-Japan studies are ongoing.

About Diabetic Macular Edema (DME)
DME is a common complication of Diabetic Retinopathy (DR), a disease affecting the blood vessels of the retina. Clinically significant DME occurs when fluid leaks into the center of the macula, the light-sensitive part of the retina responsible for sharp, direct vision. Fluid in the macula can cause severe vision loss or blindness.

DME is the most frequent cause of blindness in young and mid-aged adults. According to the American Diabetes Association, over 18 million Americans currently suffer from diabetes, and many more are at risk for developing diabetes. The incidence of diabetes is steadily climbing and it is projected that up to seven percent of all patients with diabetes will develop DME during their lifetime.

About EYLEA® (aflibercept) Injection for Intravitreal Injection
Vascular Endothelial Growth Factor (VEGF) is a naturally occurring protein in the body. In patients with diabetic macular edema (DME), hyperglycemia-induced vascular dysfunction and hypoxia result in elevated intraocular VEGF levels in the eye and resultant blood vessel permeability that leads to macular edema, which can result in vision loss.

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 (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 marketed for the treatment of wet AMD in over 15 countries outside the U.S., including Japan and Australia. Bayer HealthCare has received a positive recommendation for approval by the European Committee for Medicinal Products for Human Use (CHMP) for the treatment of visual impairment due to Macular Edema secondary to Central Retinal Vein Occlusion (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, allergic asthma, and atopic dermatitis. For additional information about the company, please visit 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.

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. 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 for DME; 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 product candidates; competing drugs and product candidates that may be superior to Regeneron's products and product candidates; uncertainty of market acceptance 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. 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, unless required by law.

Bayer Forward-Looking Statements
This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer Group or subgroup management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.

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