

Two Year Results of Phase 3 Studies with EYLEA™ (aflibercept) Injection in wet AMD Show Sustained Improvement in Visual Acuity

Patients in the EYLEA 2mg every eight week group achieved visual acuity gains similar to ranibizumab with 5 fewer injections, on average, over two years

Patients who required the most intense therapy received, on average, 1.4 fewer injections in the EYLEA 2mg every eight week group compared to ranibizumab in the second year

TARRYTOWN, N.Y. and BERLIN, Dec. 5, 2011 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) and Bayer HealthCare today announced that in an integrated analysis of two parallel Phase 3 studies (VIEW 1 and VIEW 2) in patients with the neovascular form of age-related macular degeneration (wet AMD), patients treated with EYLEA™ (aflibercept) Injection For Intravitreal Injection showed a sustained improvement in visual acuity at 96 weeks versus baseline. The 52-week results (primary analyses) from these studies have previously been reported.

During the first year of the VIEW 1 and VIEW 2 studies, patients were treated with three different dosing regimens of EYLEA, 0.5 milligram (mg) every four weeks, 2mg every four weeks, and 2mg every eight weeks (following three initial monthly injections), compared to ranibizumab 0.5mg every four weeks. The EYLEA 2mg every eight week regimen was recently approved by the U.S. Food and Drug Administration (FDA), based on efficacy (maintenance of vision) that was clinically equivalent at one year to the monthly ranibizumab regimen. In the second year of the studies, patients were treated with the same dose per injection as in the first year and were evaluated monthly to determine need for retreatment. Patients were treated at least every 12 weeks. All year two analyses were considered exploratory.

In an integrated analysis of the VIEW 1 and VIEW 2 studies, the visual acuity gain from baseline in the EYLEA 2mg every eight week group at week 96 was 7.6 letters compared to 8.4 letters at week 52, with an average of 11.2 injections over two years and 4.2 injections during the second year. The visual acuity gain from baseline in the monthly ranibizumab group at week 96 was 7.9 letters compared to 8.7 letters at week 52, with an average of 16.5 injections over two years and 4.7 injections during the second year. The results of each of the VIEW 1 and VIEW 2 studies were consistent with the integrated analysis.

The overall fewer average number of injections in the second year in the EYLEA 2mg every eight week group compared to the ranibizumab group (4.2 versus 4.7) was driven by the fact that fewer patients needed more intense therapy in the EYLEA group and those patients required fewer injections.

The proportion of patients who required frequent injections (six or more) during the second year was lower in the EYLEA 2mg every eight week group compared to the ranibizumab group (15.9% versus 26.5%). In the 25% of patients who required the most intense therapy (the greatest number of injections), patients in the EYLEA 2mg every eight week group required an average of 1.4 fewer injections in the second year compared to the ranibizumab group (6.6 versus 8.0). In the 25% of patients in each group who had the fewest number of injections in the second year, the average number of injections was similar (approximately 3 for both groups, corresponding to the protocol-mandated minimum number of injections).

A generally favorable safety profile was observed for both EYLEA and ranibizumab. The incidence of ocular treatment emergent adverse events was balanced across all four treatment groups in both studies, with the most frequent events associated with the injection procedure, the underlying disease and/or the aging process. The most frequent ocular adverse events (greater than 10% of patients for the overall study population) were conjunctival hemorrhage, eye pain, retinal hemorrhage, and visual acuity reduced. The most frequent serious non-ocular adverse events were typical of those reported in this elderly population who receive intravitreal treatment for wet AMD; the most frequently reported events (greater than 1% of patients for the overall study population) were falls, pneumonia, myocardial infarction and atrial fibrillation. There were no notable differences among the study arms. The incidence of arterial thrombotic events as defined by the "Anti-Platelet Trialists" group criteria was 3.2% of patients for ranibizumab and 3.3% of patients in the combined EYLEA groups.

"These second year results confirm the sustainability of the vision gains achieved by EYLEA with a less than monthly dosing frequency. Importantly, the second year data demonstrated that for patients that needed more anti-VEGF treatment, this was achieved with fewer injections using EYLEA," said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Laboratories. "As a reminder, the recommended dose for EYLEA is 2mg every eight weeks following three initial monthly injections, which demonstrated visual acuity gains that were clinically equivalent to monthly ranibizumab. Retinal physicians and their wet AMD patients consider the predictable every eight week dosing regimen for EYLEA as a significant advance that helps overcome the challenges of monthly office visits."

Further results from year two of the studies will be presented at upcoming medical conferences.

About the VIEW Program

The VIEW (VEGF Trap: Investigation of Efficacy and Safety in Wet AMD) program consists of two randomized, double-masked, Phase 3 clinical trials evaluating EYLEA in the treatment of the neovascular form of age-related macular degeneration (wet AMD). The VIEW 1 study, which randomized 1217 patients, was conducted in the United States and Canada by Regeneron. The VIEW 2 study, which randomized 1240 patients, was conducted in Europe, Asia Pacific, Japan, and Latin America by Bayer HealthCare. The study designs are essentially identical. The primary endpoint evaluation was conducted at 52 weeks.

About Wet AMD

Age-related Macular Degeneration (AMD) is a leading cause of acquired blindness. Macular degeneration is diagnosed as either dry (non-exudative) or wet (exudative). In wet AMD, new blood vessels grow beneath the retina and leak blood and fluid. This leakage causes disruption and dysfunction of the retina creating distortion and/or blind spots in central vision, and it can account for blindness in wet AMD patients. Wet AMD is the leading cause of blindness for people over the age of 65 in the U.S. and Europe.

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.

EYLEA™ (aflibercept) Injection, 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 these cognate VEGF receptors.

IMPORTANT PRESCRIBING INFORMATION

In the United States, EYLEA is indicated for the treatment of patients with neovascular age-related macular degeneration (wet AMD).

The recommended dose for EYLEA is 2 mg administered by intravitreal injection every four weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg once every eight weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every four weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every four weeks compared to every eight weeks.

IMPORTANT SAFETY INFORMATION

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.

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.

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 with EYLEA in clinical trials was low (1.8%).

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

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

Please see the full Prescribing Information for EYLEA, available online at www.regeneron.com/EYLEA-fpi.pdf.

About the EYLEA™ (aflibercept) Injection Global Collaboration

Regeneron is collaborating with Bayer HealthCare on the global development of EYLEA. Bayer submitted an application for marketing authorization in Europe for wet AMD in June 2011.

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 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 two products, ARCALYST® (riloncept) Injection For Subcutaneous Use and EYLEA™ (aflibercept) Injection. Regeneron also has completed several Phase 3 studies and is conducting an additional Phase 3 clinical trial for the product candidate ZALTRAP® (aflibercept) Concentrate for Intravenous Infusion. Additional therapeutic candidates developed from proprietary Regeneron technologies for creating fully human monoclonal antibodies are in earlier stage development programs in rheumatoid arthritis and other inflammatory conditions, pain, cholesterol reduction, allergic and immune conditions, and cancer. Additional information about Regeneron and recent news releases are available on the Regeneron web site at www.regeneron.com.

About Bayer HealthCare

The Bayer Group is a global enterprise with core competencies in the fields of health care, nutrition and high-tech materials.

Bayer HealthCare, a subgroup of Bayer AG with annual sales of more than EUR 16.913 billion (2010), 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 and manufacture products that will improve human and animal health worldwide. Bayer HealthCare has a global workforce of 55,700 employees and is represented in more than 100 countries. Find more information at www.bayerhealthcare.com.

Regeneron Forward-Looking Statement

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 EYLEA and Regeneron's product candidates and research and clinical programs now underway or planned, 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 EYLEA and other products and drug candidates, competing drugs that may be superior to EYLEA and Regeneron's products and drug candidates, uncertainty of market acceptance of EYLEA and Regeneron's products and drug candidates, unanticipated expenses, the availability and cost of capital, 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 without any 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, 2010 and Form 10-Q for the quarter ended September 30, 2011. 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.

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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