Regeneron Announces FDA Approval of EYLEA™ (aflibercept) Injection for the Treatment of Wet Age-Related Macular Degeneration: CORRECTED

November 18, 2011

In the news release, Regeneron Announces FDA Approval of EYLEA™ (aflibercept) Injection for the Treatment of Wet Age-Related Macular Degeneration, issued 18-Nov-2011 by Regeneron Pharmaceuticals, Inc. over PR Newswire, the third paragraph, second sentence, should read "EYLEA offers the potential of achieving the efficacy we've come to expect from current anti-VEGF agents, but with less frequent injections and monitoring." The complete, corrected release follows:

TARRYTOWN, N.Y., Nov. 18, 2011 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (Nasdaq: **REGN**) today announced that the U.S. Food and Drug Administration (FDA) has approved EYLEA (aflibercept) Injection, known in the scientific literature as VEGF Trap-Eye, for the treatment of patients with neovascular (wet) Age-related Macular Degeneration (AMD) at a recommended dose of 2 milligrams (mg) every four weeks (monthly) for the first 12 weeks, followed by 2 mg every eight weeks (2 months).

The approval of EYLEA was granted under a Priority Review, a designation that is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. This approval was based upon the results of two Phase 3 clinical studies. In these studies, EYLEA dosed every eight weeks, following three initial monthly injections, was clinically equivalent to the standard of care, Lucentis® (ranibizumab injection) dosed every four weeks, as measured by the primary endpoint of maintenance of visual acuity (less than 15 letters of vision loss on an eye chart) over 52 weeks. The most common adverse reactions (frequency of 5% or more) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and increased intraocular pressure. The adverse event profile was similar to that seen with ranibizumab.

"The approval of EYLEA offers a much needed new treatment option for patients with wet AMD," said Jeffrey Heier, M.D., a clinical ophthalmologist and retinal specialist at Ophthalmic Consultants of Boston, Assistant Professor of Ophthalmology at Tufts School of Medicine, and Chair of the Steering Committee for the VIEW 1 trial. "EYLEA offers the potential of achieving the efficacy we've come to expect from current anti-VEGF agents, but with less frequent injections and monitoring. This may reduce the need for costly and time-consuming monthly office visits for patients and their caregivers."

"This approval is an important step forward for Regeneron and for patients suffering with wet AMD, the most common cause of blindness in the U.S. in older adults," said Leonard S. Schleifer, M.D., Ph.D., President and Chief Executive Officer of Regeneron. "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. Now that EYLEA is approved, we plan to make EYLEA available to patients within the next few days."

About EYLEA™ (aflibercept) 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 (PlGF) and thereby can inhibit the binding and activation of these cognate VEGF receptors.

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

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.

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 and include endophthalmitis, traumatic cataract, and increased intraocular pressure.

About the VIEW 1 and VIEW 2 Clinical Studies

The safety and efficacy of EYLEA were assessed in two randomized, multi-center, double-masked, active-controlled studies in patients with wet AMD. A total of 2412 patients were treated and evaluable for efficacy (1817 with EYLEA) in the two studies (VIEW 1 and VIEW 2). In each study, patients were randomly assigned in a 1:1:1:1 ratio to one of four dosing regimens: 1) EYLEA administered 2 mg every eight weeks following three initial

monthly doses (EYLEA 2Q8); 2) EYLEA administered 2 mg every four weeks (EYLEA 2Q4); 3) EYLEA 0.5 mg administered every four weeks (EYLEA 0.5Q4); and 4) ranibizumab administered 0.5 mg every four weeks (ranibizumab 0.5Q4). Patient ages ranged from 49 to 99 years with a mean of 76 years.

In both studies, the primary efficacy endpoint was the proportion of patients who maintained vision, defined as losing fewer than 15 letters of visual acuity at week 52 compared to baseline. Data are available through week 52. Both the EYLEA™ (aflibercept) Injection 2Q8 and 2Q4 dosing groups were shown to have efficacy that was clinically equivalent to the ranibizumab 0.5Q4 group for the primary endpoint.

Select results of the VIEW 1 and VIEW 2 studies as described in the full Prescribing Information for the EYLEA 2 mg every four weeks and EYLEA 2 mg every eight weeks dosing groups as compared to ranibizumab dosed monthly group are shown below.

Efficacy Outcomes at Week 52 (Full Analysis Set with LOCF) in VIEW 1 and VIEW 2 Studies

	VIEW 1			**VIEW 2**		
	EYLEA 2 mg Q8 weeks(a)	EYLEA 2 mg Q4 weeks	ranibizu-mab 0.5 mg Q4 weeks	EYLEA 2 mg Q8 weeks(a)	EYLEA 2 mg Q4 weeks	ranibizu-mab 0.5 mg Q4 weeks
Full Analysis Set	N=301	N=304	N=304	N=306	N=309	N=291
Efficacy Outcomes						
Proportion of patients who maintained visual acuity (%) (						