EYLEA HD® (aflibercept) Injection 8 mg Phase 3 Trial Meets Primary Endpoint Showing Improved Vision with Extended Dosing Intervals in Patients with Macular Edema following Retinal Vein Occlusion

December 17, 2024 at 7:00 AM EST

EYLEA HD demonstrated non-inferior vision gains with an every 8-week dosing regimen compared to EYLEA® (aflibercept) Injection 2 mg dosed every 4 weeks

Safety data remains consistent with the known EYLEA HD and EYLEA safety profiles

Supplementary biologics license application planned for submission to the U.S. Food and Drug Administration in the first quarter of 2025

TARRYTOWN, N.Y., Dec. 17, 2024 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced the primary endpoint was met in the Phase 3 QUASAR trial investigating EYLEA HD® (aflibercept) Injection 8 mg for the treatment of patients with macular edema following retinal vein occlusion (RVO), including those with central, branch and hemiretinal vein occlusions. In the trial, patients treated with EYLEA HD every 8 weeks (after initial monthly doses) experienced non-inferior vision gains compared to those treated with the approved monthly dosing regimen of EYLEA® (aflibercept) Injection 2 mg, the current standard of care. These data will be submitted to regulatory authorities around the world, with a submission to the U.S. Food and Drug Administration (FDA) planned for the first quarter of 2025, and are planned for presentation at an upcoming medical meeting.

“All currently FDA-approved anti-VEGF therapies for retinal vein occlusion require monthly dosing, which can be burdensome for a patient. These impressive data from QUASAR demonstrated that EYLEA HD patients with retinal vein occlusion experienced improved vision with fewer injections than EYLEA – which could offer a significant advancement in this treatment setting,” said Seenu M. Hariprasad, M.D., Chair of the Department of Ophthalmology and Visual Science, The University of Chicago. “Furthermore, about 90% of EYLEA HD patients were able to maintain 8-week dosing intervals through 36 weeks.”

QUASAR is a global, double-masked, active-controlled Phase 3 trial evaluating the efficacy and safety of EYLEA HD, compared to EYLEA, in patients with RVO. EYLEA HD patients were treated with an 8-week dosing regimen (after 3 or 5 initial monthly doses), and EYLEA patients were treated every 4 weeks. The primary endpoint was met at 36 weeks, with both groups of EYLEA HD patients achieving non-inferior visual acuity gains compared to those receiving EYLEA. EYLEA HD results were consistent across patients with branch retinal vein occlusions, and those with central retinal or hemiretinal vein occlusions.

Outcomes at 36 weeks were as follows:

	EYLEA 4-week regimen (n=301)	**EYLEA HD 8-week regimen after 3 initial monthly doses (n=293)**	**EYLEA HD 8-week regimen after 5 initial monthly doses (n=298)**
Mean observed BCVA improvement	17.8 letters	17.0 letters	19.1 letters
Least squares mean difference in BCVA improvement, primary endpoint (non-inferiority p-value)*		-0.1 (p<0.0001)	0.8 (p<0.0001)
Mean observed BCVA	72.0 letters	72.8 letters	74.6 letters
Patients maintained on every 8-week dosing interval		88%	93%

BCVA: best corrected visual acuity
*Non-inferiority (1-sided) p-values are for the difference in least squares mean compared to EYLEA with margin of 4 letters. EYLEA HD groups met non-inferiority.

The safety profile of EYLEA HD (n=591) was similar to EYLEA (n=301) in QUASAR and remained generally consistent with the known safety profile of EYLEA HD in its pivotal trials. Ocular treatment emergent adverse events (TEAEs) occurring in ≥5% of all EYLEA HD patients included increased ocular pressure (5%), and there was one case each of endophthalmitis and retinal vasculitis. The rate of intraocular inflammation was 0.5% for EYLEA HD and 1.3% for EYLEA. Hypertension at baseline was present in 66% of EYLEA HD patients and 62% of EYLEA patients. Hypertension during the trial was reported in 8.1% of EYLEA HD patients and 4.7% of EYLEA patients. Thromboembolic events (APTC) occurred in 0.5% of EYLEA HD patients and 1.7% of EYLEA patients.

"With these pivotal results in retinal vein occlusion, EYLEA HD with extended dosing has again met the high bar of vision gains and safety seen with standard-of-care EYLEA," said George D. Yancopoulos, M.D., Ph.D., Board co-Chair, President and Chief Scientific Officer at Regeneron, and a principal inventor of EYLEA. "EYLEA HD has already made a significant impact on the treatment of its three approved indications – wet age-related macular degeneration, diabetic macular edema and diabetic retinopathy – and now has the potential to substantially reduce the treatment burden for patients with retinal vein occlusion. We look forward to sharing these results with regulatory authorities around the world as soon as possible."

EYLEA HD (known as Eylea™ 8 mg in the European Union and Japan) is being jointly developed by Regeneron and Bayer AG. In the U.S., Regeneron maintains exclusive rights to EYLEA and EYLEA HD. Bayer has licensed the exclusive marketing rights outside of the U.S., where the companies share equally the profits from sales of EYLEA and EYLEA HD.

The safety and efficacy of EYLEA HD for the treatment of RVO has not been evaluated by any regulatory authority.

About the QUASAR Trial
QUASAR is a global double-masked, active-controlled Phase 3 trial evaluating the efficacy and safety of EYLEA HD in patients with macular edema secondary to RVO, including those with central retinal vein occlusion, branch retinal vein occlusion, or hemiretinal vein occlusion.

In the trial, patients were randomized into three groups to receive either: EYLEA HD every 8 weeks following 3 initial monthly doses; EYLEA HD every 8 weeks following 5 initial monthly doses; or EYLEA every 4 weeks. The primary endpoint was mean change in BCVA from randomization through week 36, as measured by the Early Treatment Diabetic Retinopathy Study letter score.

Patients in the EYLEA HD groups can have their dosing intervals shortened to a minimum of every 4 weeks throughout the trial if protocol-defined criteria for disease progression are met. Dosing intervals may be extended based on protocol-defined criteria starting at week 32 for patients who receive EYLEA or EYLEA HD after 3 initial monthly doses or at week 40 for patients who receive EYLEA HD after 5 initial monthly doses, with follow-up planned through week 64.

QUASAR is being operationalized by Bayer under a collaboration agreement with Regeneron.

About Retinal Vein Occlusion
RVO is a common cause of vision loss in adults and the second most common retinal vascular disease. RVO occurs when there is a blockage in a vein in the retina, which leads to a buildup of blood, restricted blood flow, increased pressure and sometimes pain in the eye. RVO may cause sudden blurry vision or vision loss and can ultimately result in serious complications like swelling in the eye called macular edema.

A protein called vascular endothelial growth factor (VEGF) is instrumental in causing the vascular leakage that leads to macular edema. When a vein in the retina is blocked, the levels of VEGF increase, which spurs new blood vessel growth. Too much VEGF can lead to the formation of abnormal blood vessels and may cause vision to become blurry. Anti-VEGF injections are commonly used to treat macular edema due to RVO.

There are two main types of RVO: central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO). In CRVO, the buildup occurs in the eye's central retinal vein and in BRVO, the buildup occurs in one of the smaller branch veins. Globally, RVO affects over 28 million people.

About Ophthalmology at Regeneron
At Regeneron, we relentlessly pursue groundbreaking innovations in eye care science to help maintain the eye health of the millions of Americans impacted by vision-threatening conditions. Over a decade ago, our breakthrough scientific research resulted in the development of EYLEA, a vascular endothelial growth factor (VEGF) inhibitor designed to block the growth of new blood vessels and decrease the ability of fluid to pass through blood vessels in the eye. EYLEA has since brought fundamental change to the retinal disease treatment landscape and is supported by a robust body of research.

Regeneron continues to advance our anti-angiogenesis expertise with new solutions with the aim of offering optimal flexibility for a broad group of patients and eye care professionals. This includes EYLEA HD, which has been developed with the aim of extending the time between injections, while maintaining the vision gains, anatomic benefits and safety previously observed with EYLEA.

IMPORTANT SAFETY INFORMATION AND INDICATIONS

INDICATIONS

EYLEA HD® (aflibercept) Injection 8 mg is a prescription medicine approved for the treatment of patients with Wet Age-Related Macular Degeneration (AMD), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).

EYLEA® (aflibercept) Injection 2 mg is a prescription medicine approved for the treatment of patients with Wet Age-Related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR), and Retinopathy of Prematurity (ROP) (0.4 mg).

IMPORTANT SAFETY INFORMATION

- EYLEA HD and EYLEA are administered by injection into the eye. You should not use EYLEA HD or EYLEA if you have an infection in or around the eye, eye pain or redness, or known allergies to any of the ingredients in EYLEA HD or EYLEA, including aflibercept.
- Injections into the eye with EYLEA HD or EYLEA can result in an infection in the eye, retinal detachment (separation of retina from back of the eye) and, more rarely, serious inflammation of blood vessels in the retina that may include blockage. Call your doctor right away if you or your baby (if being treated with EYLEA for Retinopathy of Prematurity) experience eye pain or redness, light sensitivity, or a change in vision after an injection.
- In some patients, injections with EYLEA HD or EYLEA may cause a temporary increase in eye pressure within 1 hour of the injection. Sustained increases in eye pressure have been reported with repeated injections, and your doctor may monitor this after each injection.
- In infants with Retinopathy of Prematurity (ROP), treatment with EYLEA will need extended periods of ROP monitoring.
- There is a potential but rare risk of serious and sometimes fatal side effects, related to blood clots, leading to heart attack or stroke in patients receiving EYLEA HD or EYLEA.
- The most common side effects reported in patients receiving EYLEA HD were cataract, increased redness in the eye, increased pressure in the eye, eye discomfort, pain, or irritation, blurred vision, vitreous (gel-like substance) floaters, vitreous detachment, injury to the outer layer of the eye, and bleeding in the back of the eye.
- The most common side effects reported in patients receiving EYLEA were increased redness in the eye, eye pain, cataract, vitreous detachment, vitreous floaters, moving spots in the field of vision, and increased pressure in the eye.
- The most common side effects reported in pre-term infants with ROP receiving EYLEA were separation of the retina from the back of the eye, increased redness in the eye, and increased pressure in the eye. Side effects that occurred in adults are considered applicable to pre-term infants with ROP, though not all were seen in clinical studies.
- You may experience temporary visual changes after an EYLEA HD or EYLEA injection and associated eye exams; do not drive or use machinery until your vision recovers sufficiently.
- For additional safety information, please talk to your doctor and see the full Prescribing Information for EYLEA HD and EYLEA.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please click here for full Prescribing Information for EYLEA HD and EYLEA.

About Regeneron
Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents, develops and commercializes life-transforming medicines for people with serious diseases. Founded and led by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to numerous approved treatments and product candidates in development, most of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, neurological diseases, hematologic conditions, infectious diseases, and rare diseases.

Regeneron pushes the boundaries of scientific discovery and accelerates drug development using our proprietary technologies, such as *VelociSuite*®, which produces optimized fully human antibodies and new classes of bispecific antibodies. We are shaping the next frontier of medicine with data-powered insights from the Regeneron Genetics Center® and pioneering genetic medicine platforms, enabling us to identify innovative targets and complementary approaches to potentially treat or cure diseases.

For more information, please visit www.Regeneron.com or follow Regeneron on LinkedIn, Instagram, Facebook or X.

Forward-Looking Statements and Use of Digital Media
This press release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), 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 products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Products") and product candidates being developed by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Product Candidates") and research and clinical programs now underway or planned, including without limitation EYLEA HD® (aflibercept) Injection 8 mg; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates and new indications for Regeneron's Products, such as EYLEA HD for the treatment of patients with macular edema following retinal vein

occlusion ("RVO"); uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products and Regeneron's Product Candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary), including the studies discussed or referenced in this press release, on any of the foregoing or any potential regulatory approval of Regeneron's Products (such as EYLEA HD for the treatment of patients with RVO) and Regeneron's Product Candidates; the ability of Regeneron's collaborators, licensees, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and Regeneron's Product Candidates; the ability of Regeneron to manage supply chains for multiple products and product candidates; safety issues resulting from the administration of Regeneron's Products (such as EYLEA HD) and Regeneron's Product Candidates in patients, including serious complications or side effects in connection with the use of Regeneron's Products and Regeneron's Product Candidates in clinical trials; 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 Regeneron's Product Candidates; ongoing regulatory obligations and oversight impacting Regeneron's Products, research and clinical programs, and business, including those relating to patient privacy; the availability and extent of reimbursement of Regeneron's Products from third-party payers, including private payer healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid; coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and Regeneron's Product Candidates (including biosimilar versions of Regeneron's Products); the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators or licensees may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license, collaboration, or supply agreement, including Regeneron's agreements with Sanofi and Bayer (or their respective affiliated companies, as applicable), to be cancelled or terminated; the impact of public health outbreaks, epidemics, or pandemics (such as the COVID-19 pandemic) on Regeneron's business; and risks associated with intellectual property of other parties and pending or future litigation relating thereto (including without limitation the patent litigation and other related proceedings relating to EYLEA® (aflibercept) Injection 2 mg), other litigation and other proceedings and government investigations relating to the Company and/or its operations (including the pending civil proceedings initiated or joined by the U.S. Department of Justice and the U.S. Attorney's Office for the District of Massachusetts), the ultimate outcome of any such proceedings and investigations, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition. A more complete description of these and other material risks can be found in Regeneron's filings with the U.S. Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2023 and its Form 10-Q for the quarterly period ended September 30, 2024. Any forward-looking statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any forward-looking statements made by Regeneron. Regeneron does not undertake any obligation to update (publicly or otherwise) any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

Regeneron uses its media and investor relations website and social media outlets to publish important information about the Company, including information that may be deemed material to investors. Financial and other information about Regeneron is routinely posted and is accessible on Regeneron's media and investor relations website (https://investor.regeneron.com) and its LinkedIn page (https://www.linkedin.com/company/regeneron-pharmaceuticals).

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Source: Regeneron Pharmaceuticals, Inc.