Three-Year Results for EYLEA HD® (aflibercept) Injection 8 mg in Patients with Wet Age-related Macular Degeneration Demonstrate Continued Durable Vision Gains and Anatomic Improvements with Extended Dosing Intervals

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At three years of EYLEA HD treatment, the vast majority of patients maintained visual and anatomic improvements while achieving extended dosing regimens, including those of just twice a year: 77%, 58%, 40% and 24% achieved last assigned dosing intervals of ≥3, ≥4, ≥5 and 6 months, respectively

At three years, the vast majority of patients who switched to EYLEA HD from a fixed 2-month dosing regimen with EYLEA® (aflibercept) Injection 2 mg maintained visual and anatomic improvements while rapidly extending their dosing intervals: 79%, 43% and 16% achieved last assigned dosing intervals of ≥3, ≥4 and ≥5 months, respectively

Results add to growing body of evidence showing ability of EYLEA HD to extend dosing intervals, including previously presented data in diabetic macular edema following three years of EYLEA HD treatment in which 88%, 68%, 48% and 28% of patients achieved a last assigned dosing interval of ≥3, ≥4, ≥5 and 6 months, respectively

TARRYTOWN, N.Y., Feb. 08, 2025 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive three-year (156-week) results for EYLEA HD® (aflibercept) Injection 8 mg in patients with wet age-related macular degeneration (wAMD) from an extension study of the Phase 3 PULSAR trial. The results were presented today at the virtual Angiogenesis (Angiogenesis, Exudation, and Degeneration) 2025 annual meeting. Similar to the three-year results for the pivotal PHOTON trial in diabetic macular edema (DME), the longer-term wAMD data demonstrated the vast majority of EYLEA HD patients who entered the extension study sustained the visual gains and anatomic improvements achieved by the end of the second year, while also achieving substantially longer treatment intervals. Additionally, patients who switched from EYLEA® (aflibercept) Injection 2 mg to EYLEA HD at the beginning of the third year were also able to maintain vision and anatomic improvements through the end of the third year, but with longer dosing intervals and fewer injections.

“Patients with wet age-related macular degeneration are older and often need assistance in getting to their doctors’ offices. Reducing their treatment burden can be transformative for their care,” said W. Lloyd Clark, M.D., Palmetto Retinal Center, and Assistant Clinical Professor of Ophthalmology at the University of South Carolina School of Medicine. “Impressively, the latest three-year EYLEA HD results show a substantial portion of patients were able to sustain visual and anatomic benefits with only two doses a year. This adds yet another notable piece of evidence to an already remarkable body of data supporting EYLEA HD.”

In PULSAR, EYLEA HD patients were initially randomized at baseline to either 3- or 4-month dosing intervals (after three initial monthly doses). If pre-specified criteria were met, dosing intervals could be shortened throughout the trial or extended in the second and third years. As previously presented, 88% of all EYLEA HD patients maintained ≥3-month dosing intervals at the end of two years. Patients could then participate in an optional extension study for an additional 60 weeks. Of the EYLEA HD patients (n=375) who completed the full 3 years of treatment:

- Nearly 60% had a last assigned dosing interval of ≥4 months, with 40% and 24% having a last assigned dosing interval of ≥5 and 6 months, respectively, at the end of three years of treatment.
- Vision gains and anatomical improvements – including robust reductions in retinal thickness – that were achieved through year two were sustained through year three in the extension study.

Patients in the PULSAR comparator arm received EYLEA as a fixed 2-month dosing regimen (after three initial monthly doses) for 96 weeks. These patients had the option to enter the extension study at week 96 and were switched to a 3-month dosing interval with EYLEA HD. Of these patients who completed the extension study (n=186), vision and anatomic improvements were maintained after switching to EYLEA HD, with 79% and 43% having a last assigned dosing interval of ≥3 and ≥4 months, respectively, at week 156.

The safety profile of EYLEA HD continued to be similar to EYLEA through three years and remained generally consistent with the known safety profile of EYLEA HD in its pivotal trials. Ocular treatment emergent adverse events (TEAEs) occurring in ≥4% of all patients included cataract, retinal hemorrhage, reduction of visual acuity, vitreous floaters, and increase of intraocular pressure. The rate of intraocular inflammation was 2.4% for the patients that switched from EYLEA to EYLEA HD, and 1.9% for the EYLEA HD patients randomized at baseline.

The three-year data from the PHOTON trial for EYLEA HD in DME were previously presented at the American Academy of Ophthalmology annual meeting in October 2024.

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.

About the EYLEA HD Clinical Trial Program
PULSAR in wAMD and PHOTON in DME/diabetic retinopathy (DR) are double-masked, active-controlled pivotal trials that were conducted in multiple centers globally. In both trials, patients were randomized into 3 treatment groups to receive either: EYLEA HD every 3 months, EYLEA HD every 4 months, or EYLEA every 2 months. The lead sponsors of the trials were Bayer for PULSAR and Regeneron for PHOTON.

Patients treated with EYLEA HD in both trials had 3 initial monthly doses, and patients treated with EYLEA received 3 initial doses in PULSAR and 5 in PHOTON. In the first year, patients in the EYLEA HD groups could have their dosing intervals shortened down to an every 2-month interval if protocol-defined criteria for disease progression were observed. Intervals could not be extended until the second year of the trial. Patients in all EYLEA groups maintained a fixed 2-month dosing regimen throughout their participation in the two-year trials.

In both trials, there was an optional extension study starting at week 96, with all participating patients receiving EYLEA HD through week 156. Patients initially randomized to EYLEA in PULSAR, were switched to EYLEA HD at the start of the extension study and immediately assigned to a 3-month dosing interval. Dosing intervals for all patients in the extension study could be shortened or extended by 2-week increments if protocol-defined criteria were met, with a minimum dosing interval of every 2 months and a maximum dosing interval of every 6 months.

About wAMD and Diabetic Eye Disease
wAMD is a retinal disease that may affect people as they age. It occurs when abnormal blood vessels grow and leak fluid under the macula, the part of the eye responsible for sharp central vision and seeing fine detail. This fluid can damage and scar the macula, which can cause vision loss. An estimated 1.4 million Americans have wAMD.

DR is an eye disease characterized by microvascular damage to the blood vessels in the retina often caused by poor blood sugar control in people with diabetes. The disease generally starts as nonproliferative diabetic retinopathy (NPDR) and often has no warning signs or symptoms. NPDR may progress to proliferative diabetic retinopathy (PDR), a stage of the disease in which abnormal blood vessels grow onto the surface of the retina and into the vitreous cavity, potentially causing severe vision loss.

DME can occur at any stage of DR as the blood vessels in the retina become increasingly fragile and leak fluid, potentially causing visual impairment. In the U.S., approximately 1.5 million adults are diagnosed with DME, while approximately 6 million people have DR without DME.

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; 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; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates and new indications for Regeneron's Products; 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; changes in laws, regulations, and policies affecting the healthcare industry; 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 on Regeneron's business; and risks associated with 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), 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), 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, 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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