Three-year Results for EYLEA HD® (aflibercept) Injection 8 mg Demonstrate Continued Durable Vision Gains and Anatomic Improvements with Extended Dosing Intervals in Patients with Diabetic Macular Edema

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88% of EYLEA HD patients had a last assigned dosing interval of ≥12 weeks at week 156, while sustaining visual and anatomic improvements achieved in the first 96 weeks, in this extension study of the Phase 3 PHOTON trial presented at AAO

Patients switched to EYLEA HD experienced substantially slower fluid reaccumulation, as compared to their previous rate of fluid reaccumulation with EYLEA® (aflibercept) Injection 2 mg

The consistent achievement of much longer dosing intervals with EYLEA HD – together with the notably slower fluid reaccumulation observed following switch to EYLEA HD – supports the longer duration of action of EYLEA HD versus EYLEA

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

TARRYTOWN, N.Y., Oct. 18, 2024 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive three-year (156-week) data for EYLEA HD® (aflibercept) Injection 8 mg from an extension study of the Phase 3 PHOTON trial in patients with diabetic macular edema (DME). At three years, the longer-term data showed 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 achieving substantially longer treatment intervals than have been previously demonstrated. Notably, patients switched to EYLEA HD experienced substantially slower fluid reaccumulation following their first EYLEA HD dose. The achievement of much longer dosing intervals with EYLEA HD – together with the notably slower fluid reaccumulation – supports the longer duration of action of EYLEA HD. The results were presented today in a late-breaking session at the American Academy of Ophthalmology (AAO) Annual meeting.

“Many patients with diabetic eye disease are of working age and often have to juggle a high burden of healthcare appointments and treatments alongside job and family commitments. These latest three-year results from the Phase 3 PHOTON trial continue to demonstrate that EYLEA HD can safely provide meaningful and lasting vision and anatomical benefits for people living with diabetic macular edema – with as few as three or four injections per year,” said Diana V. Do, M.D., Professor of Ophthalmology and Vice Chair for Clinical Affairs at the Byers Eye Institute, Stanford University and a trial investigator. “Over the last year, EYLEA HD has made an impact on how diabetic eye disease is managed among retina specialists, and these longer-term results reinforce confidence in initiating patients on EYLEA HD as a first-line treatment.”

In PHOTON, EYLEA HD patients were initially randomized at baseline to either 12- or 16-week 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 year. As previously presented, 89% of all EYLEA HD patients completing week 96 maintained ≥12-week dosing intervals. Patients could then participate in an optional extension study for an additional 60 weeks. Of the EYLEA HD patients (n=152) who completed the full 156 weeks of treatment:

- 88% were assigned a dosing interval of ≥12 weeks, and 48% were assigned a dosing interval of ≥20 weeks, at the end of three years of treatment.
- Vision gains and anatomical improvements achieved through year two in PHOTON were sustained through year three in the extension study.

Patients in the PHOTON comparator arm received EYLEA® (aflibercept) Injection 2 mg as a fixed 8-week dosing regimen (after five initial monthly doses) for 96 weeks. These patients were then able to enter the extension study at week 96 and switch to a 12-week dosing interval with EYLEA HD. Of these patients who completed the extension study (n=58), 83% had a last assigned dosing interval ≥12 weeks at the end of the study (week 156), while mean visual and anatomic improvements achieved with EYLEA in the first 96 weeks were sustained following the switch to longer dosing intervals with EYLEA HD. Notably, patients synchronously switched to the EYLEA HD dose experienced substantially slower fluid reaccumulation following their first dose – as compared to their previous rate of fluid reaccumulation while on EYLEA treatment. The consistent achievement of much longer dosing intervals with EYLEA HD – together with the notably slower fluid reaccumulation observed following switch to EYLEA HD – support the longer duration of action of EYLEA HD versus EYLEA.

In the extension study, the safety profile of EYLEA HD (n=265) 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, vitreous floaters, and diabetic retinal edema. There were no cases of occlusive retinal vasculitis. The rate of intraocular inflammation was 1.4% for the patients that switched from EYLEA to EYLEA HD, and 1.5% for the EYLEA HD patients randomized at baseline. Anti-platelet trialists' collaboration-defined arterial thromboembolic TEAEs occurred in 7% of patients in both groups.

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 wet age-related macular degeneration 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 12 weeks, EYLEA HD every 16 weeks, or EYLEA every 8 weeks. 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 8-week interval if protocol-defined criteria for disease progression were observed. Intervals could not be extended until the second year of the study. Patients in all EYLEA groups maintained a fixed 8-week dosing regimen throughout their participation in the two-year trials.

In both studies, 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 PHOTON, were switched to EYLEA HD at the start of the extension study and immediately assigned to a 12-week 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 8 weeks and a maximum dosing interval of every 24 weeks.

About Diabetic Eye Disease
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.

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 that includes eight pivotal Phase 3 trials, 12 years of real-world experience, and more than 80 million EYLEA injections globally.

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 and EYLEA® (aflibercept) Injection 2 mg; uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products (such as EYLEA HD and EYLEA) 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 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 (such as EYLEA HD and EYLEA) 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; 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), 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 June 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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