EYLEA HD® (aflibercept) Injection 8 mg Data at EURETINA Reinforce Long-term Durability, Sustained Fluid Control and Safety Profile

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Three new post-hoc analyses highlight EYLEA HD rapid and sustained fluid control and consistent safety profile over two years in patients with wet age-related macular degeneration (wAMD)

New indirect comparison evaluates disease control of EYLEA HD and faricimab across different pivotal Phase 3 trials in wAMD

TARRYTOWN, N.Y., Sept. 11, 2024 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced new analyses of EYLEA HD® (aflibercept) Injection 8 mg and EYLEA® (aflibercept) Injection 2 mg will be presented at the Annual Meeting of the European Society of Retina Specialists (EURETINA) in Barcelona from September 19 to 22, 2024.

"The presentations at EURETINA reinforce the efficacy and safety profile of EYLEA HD and the ability to extend dosing intervals leading to significant and positive impacts on patients with wet age-related macular degeneration and diabetic macular edema," said Boaz Hirshberg, MD, Senior Vice President, Clinical Development, Internal Medicine at Regeneron. "EYLEA HD continues on its way to becoming the new standard of care for these retinal diseases based on its differentiated clinical profile, and its strong familiarity and satisfaction among retinal specialists."

Among the presentation highlights are several new post-hoc analyses of the pivotal PULSAR trial for EYLEA HD in wet age-related macular degeneration (wAMD). These include first-time oral presentations of:

- An analysis applying disease activity criteria from the faricimab Phase 3 wAMD trials to EYLEA HD to evaluate the impact on the decision for extended dosing intervals.
- An analysis evaluating the impact of EYLEA HD on sustained fluid control throughout two years of treatment as measured by central retinal thickness and best-corrected visual acuity.
- The safety of EYLEA HD from an analysis evaluating intraocular pressure outcomes through week 96.

Additional data to be shared at the meeting include analyses of the PHOTON trial in diabetic macular edema and a pooled safety analysis across the CANDELA, PHOTON and PULSAR trials.

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 following any regulatory approvals.

The following abstracts for EYLEA HD and EYLEA will be presented at EURETINA:

Abstract title	Lead author	Presentation date, time (CEST), location
EYLEA HD		
A 96-week PULSAR subgroup analysis: similar visual and anatomic improvements with aflibercept 8 mg every 12 weeks or longer and 2 mg every 8 weeks, as defined by baseline BCVA, CRT, CNV type, and race	Jean-Francois Korobelnik, MD	Oral Presentation in Free Paper Session Date: September 19 Time: 12:06–12:12 CEST Session 3: AMD
Intraocular pressure outcomes with intravitreal aflibercept 8 mg and 2 mg in patients with neovascular age-related macular degeneration through Week 96 of the PULSAR trial	Paolo Lanzetta, MD	Oral Presentation at Speakers' Corner Date: September 19 Time: 13:50–13:55 CEST Session 2: AMD
A PULSAR phase 3 trial post-hoc analysis: Evaluating the timing and magnitude of control of disease activity with aflibercept 8 mg and faricimab, applying similar disease activity criteria across different pivotal Phase 3 trials for nAMD	Michael Stewart, MD	Oral Presentation in Free Paper Session Date: September 19 Time: 16:48–16:54 CEST Session 5: AMD
A 96-week PULSAR Phase 3 trial post-hoc analysis: Rapid and sustained fluid control with aflibercept 8mg every 12 weeks or longer, as defined by fluid-free status at Weeks 16, 48, and 96 stratified by baseline CRT and BCVA	Praveen J Patel, MD	Oral Presentation in Free Paper Session Date: September 19 Time: 15:24–15:30 CEST Session 4: AMD

Impact of baseline central retinal thickness on vision among patients with diabetic macular edema: post hoc analysis of the Phase 2/3 PHOTON trial	David Lally, MD	Oral Presentation in Free Paper Session Date: September 20 Time: 9:06–9:12 CEST Session 6: Diabetes & Vascular Diseases
Pooled safety analysis of the CANDELA, PHOTON, and PULSAR trials up to 96 weeks demonstrates comparable safety profiles with aflibercept 8 mg and 2 mg	Andreas Stahl, MD	Audio-Narrated Free Paper Abstract Available on terminals throughout congress
Week 48 outcomes in aflibercept 8 mg and 2 mg treated patients by prior DME treatment status: a subgroup analysis of the Phase 2/3 PHOTON trial	Marion Munk, MD, PhD	Audio-Narrated Free Paper Abstract Available on terminals throughout congress
Intravitreal aflibercept 8 mg for diabetic macular edema: week 96 efficacy outcomes by baseline characteristics in the Phase 2/3 PHOTON trial	Deepali Varma, MD	Audio-Narrated Free Paper Abstract Available on terminals throughout congress
Outcomes of patients with DME and baseline BCVA of 20/50 or worse, and 20/40 or better who were treated with aflibercept 8 mg and 2 mg: a post-hoc analysis of the Phase 2/3 PHOTON trial	Justus G. Garweg, MD	Audio-Narrated Free Paper Abstract Available on terminals throughout congress
Intraocular pressure outcomes with aflibercept 8 mg and 2 mg in patients with diabetic macular edema through week 48 of the Phase 2/3 PHOTON trial	Dilraj S. Grewal, MD	Audio-Narrated Free Paper Abstract Available on terminals throughout the congress
Key baseline disease characteristics in nAMD are not linked to treatment interval extension of aflibercept 8 mg: a post-hoc 96-week PULSAR analysis	Javier Zarranz-Ventura, MD	Audio-Narrated Free Paper Abstract Available on terminals throughout congress
Comparable efficacy and safety with aflibercept 8 mg at extended dosing intervals beyond q16 versus 2 mg q8 in Asian patients with nAMD in PULSAR through Week 96	Timothy Lai, MD	Free Paper Session Date: September 20 Time: 11:48–11:54 CEST Session 2: AMD
Aflibercept 8 mg monotherapy results in regression of polypoidal lesions that is maintained over 96 weeks in patients with PCV in the PULSAR Phase 3 trial	Rufino Silva, MD	Free Paper Session Date: September 20 Time: 8:30–8:36 CEST Session 1: AMD
EYLEA		
Efficacy and safety outcomes from the FIREFLEYE next study of children 3 years of age with retinopathy of prematurity treated with intravitreal aflibercept versus laser in the randomized FIREFLEYE study	Andreas Stahl, MD	Oral Presentation Date: September 20 Time: 12:15-12:20 CEST Session: Results of Clinical Trials and Late Breaking Session
The XTEND study: 3-year results from a global observational study investigating proactive dosing regimens with intravitreal aflibercept 2 mg in neovascular age-related macular degeneration in routine clinical practice	Clare Bailey, MD	Audio-Narrated Free Paper Abstract Available on terminals throughout congress
Final, 3-year results from the 8 highest recruiting countries included in the global, observational XTEND study of real-world proactive regimens with intravitreal aflibercept 2 mg in patients with neovascular age-related macular degeneration	Jean-Francois Korobelnik, MD	Audio-Narrated Free Paper Abstract Available on terminals throughout congress

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 are being 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 trials.

CANDELA was a Regeneron-sponsored Phase 2 trial investigating the safety and efficacy of EYLEA HD extended dosing regimens compared to EYLEA in wAMD patients.

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 70 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 (as well as additional analyses of such 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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