EYLEA® HD (aflibercept) Injection 8 mg Presentations at ARVO Reinforce Sustained and Clinically Meaningful Outcomes in Serious Retinal Diseases

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Long-term data and subgroup analyses from pivotal EYLEA HD clinical program continue to demonstrate durable efficacy and consistent safety in patients with wet age-related macular degeneration and certain diabetic eye diseases

TARRYTOWN, N.Y., April 29, 2024 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced the presentation of positive long-term results and subgroup analyses from the pivotal clinical program of EYLEA® HD (aflibercept) Injection 8 mg. The presentations are part of 14 accepted abstracts on EYLEA HD and EYLEA® (aflibercept) Injection 2 mg that will be shared at the Association for Research in Vision and Ophthalmology (ARVO) annual meeting from May 5 to 9 in Seattle.

“Our extensive data presentations at ARVO showcase the differentiated efficacy, safety and durability of EYLEA HD, and demonstrate our commitment to advancing retinal care for patients who are at risk of losing vision,” said Boaz Hirshberg, M.D., Senior Vice President, Clinical Development, Internal Medicine at Regeneron. “Since its FDA approval, we have seen growing use and positive patient and physician experiences with EYLEA HD in both treatment-experienced and treatment-naïve patients. The ARVO presentations highlight the encouraging real-world impact of EYLEA HD seen so far and reinforce its potential as a new standard-of-care for people living with wet age-related macular degeneration, diabetic macular edema and diabetic retinopathy.”

Notable podium presentations at ARVO include:

- One-year (48 week) data from the PHOTON trial investigating EYLEA HD in diabetic macular edema (DME) patients with or without prior treatment, compared to EYLEA.
- Two-year (96 week) results from the PULSAR trial investigating EYLEA HD in patients with wet age-related macular degeneration (wAMD), compared to EYLEA, which will feature a post-hoc analysis on the correlation of key baseline disease characteristics in wAMD to dosing intervals of EYLEA HD.
- A PULSAR subgroup analysis evaluating visual and anatomic improvements with EYLEA HD, compared to EYLEA, based on baseline best corrected visual acuity (BCVA), corneal refractive therapy (CRT), choroidal neovascularization (CNV) type and race.

In addition, a population pharmacokinetics analysis will be presented to elucidate the observed extended durability of EYLEA HD compared to EYLEA. These data provide a biological rationale for the approved extended dosing regimens of EYLEA HD.

The most common adverse reactions (≥3%) reported in patients treated with EYLEA HD were cataract, conjunctival hemorrhage, intraocular pressure increased, ocular discomfort/eye pain/eye irritation, vision blurred, vitreous floaters, vitreous detachment, corneal epithelium defect, and retinal hemorrhage.

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

EYLEA HD and EYLEA presentations at ARVO:

Abstract title	Abstract	Lead author	Presentation date, time (PST), location
EYLEA HD			
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	#4887 Podium Presentation	Nitish Mehta, M.D.	Wednesday, May 8 3:45 – 4:00 PM 6E - Arch Building
BCVA gains with aflibercept 8 mg maintained through Week 96 in PULSAR with extended treatment intervals in patients with nAMD*	#2115 Podium Presentation	Sobha Sivaprasad, M.D.	Monday, May 6 3:30 – 3:45 PM 6E, Arch Building
Key baseline disease characteristics in nAMD are not linked to treatment interval extension of aflibercept 8 mg: A post-hoc 96-week PULSAR analysis*	#2116 Podium Presentation	Justus G. Garweg, M.D.	Monday, May 6 3:45 – 4:00 PM 6E, Arch Building

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*	#4906 Podium Presentation	Richard Gale, M.D.	Wednesday, May 8 3:15 – 3:30 PM 612, Arch Building
Population pharmacokinetic modeling and simulation of ocular clearance for aflibercept 8 mg and 2 mg and association with durability of effect	#A0441 Poster Presentation	Peter K. Kaiser, M.D.	Tuesday, May 7 8:30 – 10:15 AM Exhibit Hall
Impact of baseline central retinal thickness (CRT) on vision among patients with diabetic macular edema (DME): post hoc analysis of the Phase 2/3 PHOTON trial	#B0129 Poster Presentation	Deepak Sambhara, M.D.	Thursday, May 9 11:45 AM – 1:30 PM Exhibit Hall
Intraocular pressure outcomes with intravitreal injection of aflibercept 8 mg and 2 mg in patients with diabetic macular edema through Week 48 of the Phase 2/3 PHOTON trial	#B0130 Poster Presentation	Mark R. Barakat, M.D.	Thursday, May 9 11:45 AM – 1:30 PM Exhibit Hall
Outcomes of patients with diabetic macular edema (DME) and baseline best-corrected visual acuity (BCVA) of 20/50 or worse or 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	#B0148 Poster Presentation	Sean Adrean, M.D.	Thursday, May 9 11:45 AM – 1:30 PM Exhibit Hall
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*	#B0280 Poster Presentation	Andreas Stahl, M.D.	Sunday, May 5 8:00 – 9:45 AM Exhibit Hall
Aflibercept 8 mg monotherapy shows maintained efficacy over 96 weeks, with the ability to extend dosing intervals beyond every 16 weeks, in patients with PCV in the PULSAR Phase 3 trial*	#B0282 Poster Presentation	Rufino Silva, M.D.	Sunday, May 5 8:00 – 9:45 AM Exhibit Hall
Comparable efficacy with aflibercept 8 mg at extended dosing intervals beyond q16 versus 2 mg q8 in Asian patients with nAMD in PULSAR through Week 96*	#B0283 Poster Presentation	Xiaodong Sun, M.D.	Sunday, May 5 8:00 – 9:45 AM Exhibit Hall
EYLEA			
Baseline (BL) factors associated with no improvement in Diabetic Retinopathy Severity Scale (DRSS) Score in sham patients from PANORAMA over 2 years	#4928 Podium Presentation	Anita Barikian, M.D.	Wednesday, May 8 2:15 – 2:30 PM Yakima 1, Arch Building
Outcomes of retinal neurodegenerative changes in patients with diabetic macular edema from the VISTA study	#B0170 Poster Presentation	Mustafa Iftikhar, M.D.	Thursday, May 9 11:45 AM – 1:30 PM Exhibit Hall
Impact of exposure to residual intraretinal fluid and fluctuations of central subfield thickness on visual outcomes in eyes with macular edema following central retinal vein occlusion: A 1-year post hoc analysis of the COPERNICUS and GALILEO trials	#B0369 Poster Presentation	Michael S. Ip, M.D.	Sunday, May 5 1:00 – 2:45 PM Exhibit Hall

**Bayer-run trial*

About the EYLEA HD Clinical Trial Program
PULSAR in wAMD and PHOTON in DME 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. One-year results from the PULSAR and PHOTON trials were recently published in *The Lancet*.

Two-year data from the pivotal PULSAR trial were originally presented at the EURETINA Congress in October 2023, and two-year data from the pivotal PHOTON trial were first presented at the American Society of Retina Specialists annual meeting in July 2023.

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 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.

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, 11 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) 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) 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 and retinal detachment (separation of retina from back of the eye) can occur. Inflammation in the eye has been reported with the use of EYLEA HD and EYLEA.
- 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.
- Contact your doctor right away if you think you or your baby might be experiencing any side effects, including eye pain or redness, light sensitivity, or blurring of vision, after an injection.
- 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 for over 35 years by physician-scientists, our unique ability to

repeatedly and consistently translate science into medicine has led to numerous FDA-approved treatments and product candidates in development, almost all 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, hematologic conditions, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary VelociSuite® technologies, such as VelocImmune®, which uses unique genetically humanized mice to produce optimized fully human antibodies and bispecific antibodies, and through ambitious research initiatives such as the Regeneron Genetics Center®, which is conducting one of the largest genetics sequencing efforts in the world.

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

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, 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. 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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