

REGENERON

EYLEA HD (afibercept) Injection 8 mg Approved by FDA for Treatment of Wet Age-related Macular Degeneration (wAMD), Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR)

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Approval based on the pivotal PULSAR and PHOTON trials in which EYLEA[®] HD demonstrated clinically equivalent vision gains to EYLEA (afibercept) Injection 2 mg that were maintained with fewer injections

First and only treatment approved in wAMD and DME for immediate dosing at 8-week and up to 16-week intervals following three initial monthly doses

TARRYTOWN, N.Y., Aug. 18, 2023 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced that the U.S. Food and Drug Administration (FDA) has approved EYLEA HD (afibercept) Injection 8 mg for the treatment of patients with wet age-related macular degeneration (wAMD), diabetic macular edema (DME) and diabetic retinopathy (DR). The recommended dose for EYLEA HD is 8 mg (0.07 mL of 114.3 mg/mL solution) every 4 weeks (monthly) for the first 3 months across all indications, followed by 8 mg every 8 to 16 weeks (2 to 4 months) in wAMD and DME and every 8 to 12 weeks (2 to 3 months) for DR.

"The FDA approval of EYLEA HD is an important advancement in retinal care," said Peter Kaiser, M.D., Chaney Family Endowed Chair in Ophthalmology Research at the Cole Eye Institute and Professor of Ophthalmology at Cleveland Clinic Lerner College of Medicine. "With EYLEA HD, patients with wet age-related macular degeneration or diabetic retinal disease can now receive less frequent injections after their initial monthly doses and still experience the similar visual gains, anatomic improvements and safety profile of EYLEA."

"I look forward to offering EYLEA HD to my patients as a new treatment option that builds off of the established efficacy and safety profile of EYLEA," said Allen C. Ho M.D., Director of Retina Research and Co-Director of the Retina Service of Wills Eye Hospital and Professor of Ophthalmology at Thomas Jefferson University. "In its clinical trial program, EYLEA HD demonstrated an unprecedented ability to maintain vision with extended dosing intervals, which created an exciting new advancement in the treatment of our patients with serious retinal diseases."

The FDA approval is based on the 48-week results of PULSAR and PHOTON – two double-masked, active-controlled pivotal trials evaluating EYLEA HD compared to EYLEA (afibercept) Injection 2 mg. Both the PULSAR trial in wAMD (N=1,009) and PHOTON trial in DME (N=658) met their primary endpoint, with EYLEA HD demonstrating non-inferior and clinically equivalent vision gains at 48 weeks with both 12- and 16-week dosing regimens after only 3 initial monthly doses, compared to an EYLEA 8-week dosing regimen after initial monthly doses (3 in PULSAR and 5 in PHOTON). The vast majority of patients randomized at baseline to EYLEA HD 12- or 16-week dosing regimens (following 3 initial monthly doses) were able to maintain these dosing intervals through 48 weeks.

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.

"More than 10 years ago, we fundamentally changed the way that certain serious retinal diseases were treated with the introduction of EYLEA. With the approval of EYLEA HD, we have elevated the high standard that EYLEA set," said George D. Yancopoulos, M.D., Ph.D., Board co-Chair, President and Chief Scientific Officer at Regeneron, and a principal inventor of EYLEA. "Our continued commitment to retinal diseases resulted in an important scientific innovation – evolving the proven efficacy and safety of EYLEA into a new treatment, EYLEA HD, that provides lasting vision control with even fewer injections to further benefit those living with wet age-related macular degeneration or diabetic retinal diseases."

Regeneron is committed to helping patients who have been prescribed EYLEA HD access their medication. EYLEA 4U helps patients understand how EYLEA HD may be covered by their health insurance plans and assists eligible patients who need financial assistance for their EYLEA HD prescription. For more information, please call 1-855-EYLEA4U (1-855-395-3248) Option 4, or visit www.EYLEAHD.com.

EYLEA HD 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.

Regulatory filings for afibercept 8 mg are under review in Europe and Japan. Submissions to other regulatory authorities in additional countries are also planned.

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 were first [presented](#) at the American Academy of Ophthalmology annual meeting in September 2022. Topline two-year results for [PHOTON](#) and [PULSAR](#) were shared in 2023.

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 64 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 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. Regeneron's 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[™] (afibercept) Injection 8 mg for the treatment of patients with wet age-related macular degeneration, diabetic macular edema, and diabetic retinopathy; uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products (such as EYLEA HD) 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) 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[®] (afibercept) Injection 2 mg and REGEN-COV[®] (casirivimab and imdevimab)), 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, 2022 and its Form 10-Q for the quarterly period ended June 30, 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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