EYLEA® (aflibercept) Injection Approved as the First Pharmacologic Treatment for Preterm Infants with Retinopathy of Prematurity (ROP) by the FDA

February 8, 2023

ROP is a leading cause of childhood blindness worldwide

EYLEA now approved to treat five retinal conditions caused by ocular angiogenesis

TARRYTOWN, N.Y., Feb. 08, 2023 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced that the U.S. Food and Drug Administration (FDA) has approved EYLEA® (aflibercept) Injection to treat preterm infants with retinopathy of prematurity (ROP). Following this first pediatric approval, EYLEA is now indicated to treat five retinal conditions caused by ocular angiogenesis.

"Retinopathy of prematurity is a leading cause of childhood blindness worldwide. Until now, the only FDA-approved treatment in common use was laser photocoagulation, a complex and lengthy procedure that permanently ablates retina tissue and is stressful not only for infant patients but also the family navigating a delicate time after a preterm birth," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer of Regeneron, and a principal inventor of EYLEA. "For the first time, physicians will now have an FDA approved medication in EYLEA to treat this heartbreaking disease in these smallest of patients. We thank the investigators and the many families who participated in the clinical trials."

Each year in the U.S., between 1,100 to 1,500 infants develop ROP that is severe enough to require medical treatment. This rare eye disease often impacts infants who are born before 31 weeks of pregnancy have been completed or who weigh less than 1,500 grams (3.3 lbs) pounds at birth. As retinal blood vessels are often only fully developed once an infant is full-term (~9 months of pregnancy), these infants are at risk of developing retinal blood vessels that are abnormal (retinal neovascularization) potentially leading to retinal detachment and irreversible vision loss. Mild cases of ROP may improve without treatment, but some cases require treatment to keep ROP from causing significant visual impairment and even blindness.

"With no existing FDA approved guidance for the treatment of retinopathy of prematurity with anti-VEGF therapies, there was a significant need for research to understand how best to treat the disease in a manner that puts patient safety first and preserves vision for a lifetime," said Jeff Todd, Chief Executive Officer, Prevent Blindness. "Regeneron's trials investigating EYLEA in retinopathy of prematurity have advanced our understanding of how to treat this disease and provided a needed evidence-based treatment option to potentially help preterm infants preserve their vision."

About the Phase 3 Program in ROP
The FDA approval is supported by data from two randomized global Phase 3 trials – FIREFLEYE (N=113) and BUTTERFLEYE (N=120) – investigating EYLEA 0.4 mg versus laser photocoagulation (laser) in infants with ROP. In both trials, approximately 80% of EYLEA-treated infants achieved an absence of both active ROP and unfavorable structural outcomes at 52 weeks of age, which is better than would have been expected without treatment.

No new EYLEA safety signals were observed in either trial. Comparing EYLEA to laser, ocular adverse events (AEs) among patients occurred in 39% versus 37% in FIREFLEYE and 18% versus 26% in BUTTERFLEYE, with serious ocular AEs occurring in 8% for both groups in FIREFLEYE and 6.5% versus 11% in BUTTERFLEYE. AEs in both trials were consistent with infant prematurity or to the injection procedure, and with the AEs in similar ROP trials. The results of FIREFLEYE were published in Journal of the American Medical Association, and data from BUTTERFLEYE were presented at ROP Update 2022 meeting in the U.S.

Both trials were conducted pursuant to FDA Pediatric Written Request, and a Pediatric Exclusivity Determination was granted by FDA on October 12, 2022. This grant extends the period of U.S. market exclusivity for EYLEA by an additional six months through May 17, 2024.

EYLEA is being jointly developed by Regeneron and Bayer. The lead sponsors of the trials were Regeneron for BUTTERFLEYE and Bayer for FIREFLEYE. Bayer and Regeneron are collaborating on the global development of EYLEA. Regeneron maintains exclusive rights of EYLEA in the United States. Bayer has licensed the exclusive marketing rights outside the United States, where the companies share equally the profits from sales of EYLEA.

About EYLEA
EYLEA is a VEGF inhibitor formulated as an injection for the eye. It is designed to block the growth of new blood vessels and decrease the ability of fluid to pass through blood vessels (vascular permeability) in the eye by blocking VEGF-A and placental growth factor (PLGF), two growth factors involved in ocular angiogenesis. The EYLEA safety and efficacy profile is supported by a robust body of research that includes eight pivotal Phase 3 trials, more than 11 years of real-world experience and greater than 57 million EYLEA injections globally.

IMPORTANT SAFETY INFORMATION AND INDICATIONS FOR EYLEA

- EYLEA® (aflibercept) Injection is a prescription medicine administered by injection into the eye. You should not use 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, including aflibercept.
- Injections into the eye with 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.
- In some patients, injections with 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.
- The most common side effects reported in adult patients receiving EYLEA were increased redness in the eye, eye pain, cataract, vitreous (gel-like substance) 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 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.

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.

INDICATIONS

EYLEA® (aflibercept) Injection 2 mg (0.05 mL) 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).

Please see the full Prescribing Information for 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 nine FDA-approved treatments and numerous 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, pain, 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 Twitter.

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 impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, and suppliers and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs, Regeneron's ability to manage its supply chain, net product sales of products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of 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® (aflibercept) Injection for the treatment of preterm infants with retinopathy of prematurity; 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 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; 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 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; 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 or

collaboration agreement, including Regeneron's agreements with Sanofi and Bayer (or their respective affiliated companies, as applicable), to be cancelled or terminated; 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, Praluent® (alirocumab), 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, 2021 and its Form 10-Q for the quarterly period ended September 30, 2022. 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 (http://newsroom.regeneron.com) and its Twitter feed (http://twitter.com/regeneron).

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