EYLEA® (aflibercept) Injection sBLA for Every 16-week Dosing Regimen in Patients with Diabetic Retinopathy Accepted for FDA Review

June 29, 2022

If approved, extended regimen would provide a longer treatment interval and additional dosing flexibility, alongside approved every 4- and 8-week dosing regimens

TARRYTOWN, N.Y., June 29, 2022 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced the U.S. Food and Drug Administration (FDA) has accepted for review the EYLEA® (aflibercept) Injection supplemental Biologics License Application (sBLA) for an every 16-week 2 mg dosing regimen (after initial monthly doses) in patients with diabetic retinopathy (DR). The target action date for the FDA decision is February 28, 2023.

DR is the leading cause of blindness among working-age American adults, affecting more than 8 million people in the U.S. alone. In 2019, EYLEA was approved for the treatment of all stages of DR with a dosing regimen of every 4 or 8 weeks after five initial monthly doses. If approved, the 16-week dosing regimen could offer certain patients a potentially longer treatment interval and doctors with greater flexibility to individualize treatment.

The sBLA is supported by data from the Phase 3 PANORAMA trial investigating every 8- and 16-week EYLEA dosing regimens, versus sham, in patients with severe non-proliferative diabetic retinopathy (NPDR) without diabetic macular edema (DME). The submission was further supported by data from the NIH-sponsored Protocol W trial investigating an EYLEA every 16-week dosing regimen in patients with moderate to severe NPDR without center-involved DME versus sham.

At 1 year, PANORAMA met its primary endpoint of proportion of patients with ≥2-step improvement in Diabetic Retinopathy Severity Scale (DRSS) score. At 2 years, in both the PANORAMA and Protocol W trials, a greater proportion of patients receiving EYLEA every 16-weeks experienced a ≥2-step improvement in DRSS score, along with greater reductions in the risk of developing vision-threatening complications, versus sham. The rates of serious ocular adverse events and intraocular inflammation in patients treated with EYLEA every 16 weeks were similar across both studies.

In addition to DR with a 4- or 8-week dosing regimen, EYLEA is approved for the treatment of neovascular (Wet) age-related macular degeneration, macular edema following retinal vein occlusion and DME. The potential use of the 16-week dosing regimen for EYLEA in DR has not been fully evaluated by any regulatory authority.

About Diabetic Retinopathy (DR)
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 NPDR and often has no warning signs or symptoms. NPDR may progress to 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 3.5 million people have DR without DME.

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 angiogenesis. The EYLEA safety and efficacy profile is supported by a robust body of research that includes eight pivotal Phase 3 trials, 10 years of real-world experience and more than 50 million EYLEA injections globally.

IMPORTANT EYLEA INDICATIONS AND SAFETY INFORMATION

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), and Diabetic Retinopathy (DR).

- 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.
- 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 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.
- 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 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.

Please see the full Prescribing Information for EYLEA.

About Regeneron
Regeneron is a leading biotechnology company that invents, develops and commercializes life-transforming medicines for people with serious diseases. Founded and led for nearly 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, 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.

Regeneron 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; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates and new indications or dosing regimens for Regeneron's Products, such as the 16-week dosing interval for EYLEA in patients with diabetic retinopathy (including potential approval by the U.S. Food and Drug Administration based on the supplemental Biologics License Application discussed in this press release); uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products (such as 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 or any potential regulatory approval of Regeneron's Products (such as EYLEA) and Regeneron's Product Candidates; 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 (such as EYLEA) 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, including without limitation EYLEA; 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; 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, Bayer, and Teva Pharmaceutical Industries Ltd. (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, Dupixent® (dupilumab), 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 March 31, 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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