EYLEA® (aflibercept) Injection Demonstrates Positive Topline Results in Phase 3 Non-Proliferative Diabetic Retinopathy Trial

March 19, 2018

TARRYTOWN, N.Y., March 19, 2018 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today announced that the Phase 3 PANORAMA trial evaluating EYLEA® (aflibercept) Injection in moderately severe to severe non-proliferative diabetic retinopathy (NPDR) met its 24-week primary endpoint. In the trial, 58 percent of EYLEA-treated patients experienced a two-step or greater improvement from baseline on the Diabetic Retinopathy Severity Scale (DRSS) at week 24, compared to 6 percent of patients receiving sham injection (p &< 0.0001).

"This is the first time a therapy has demonstrated it can reverse disease progression in patients with moderately severe to severe non-proliferative diabetic retinopathy without diabetic macular edema, in a trial specifically designed to study this population," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer of Regeneron. "Patients in the trial continue to be evaluated to determine if EYLEA can prevent progression to neovascular vision-threatening complications or diabetic macular edema. We look forward to sharing one-year results later this year."

Patients in the active treatment groups received, on average, 4.4 EYLEA injections during the first 24 weeks. There were no new safety signals in the trial. There was one case of mild intraocular inflammation (IOI) in a patient treated with EYLEA (0.085 percent rate per injection), which is consistent with the rate of IOI seen in previous clinical trials.

About the PANORAMA trial
PANORAMA is an ongoing, pivotal, double-masked, randomized two-year trial that enrolled 402 patients and is designed to investigate EYLEA for the improvement of moderately severe to severe NPDR without diabetic macular edema (DME), compared to sham injection. Details on trial design include:

- **Three treatment arms** - An observational sham injection group and two EYLEA treatment groups. The EYLEA treatment groups started with either three or five initial monthly doses, and the trial will evaluate every eight-week dosing or every 16-week dosing at one year.
- **Two primary endpoints** - Both assess the proportion of patients who experience a two-step or greater improvement in DRSS score from baseline. The first is measured at six months (24 weeks) and the second at one year (52 weeks). The DRSS is a systematic grading scale to assess the severity of diabetic retinopathy based on photographs of the retina following a dilated eye exam.
- **Key secondary endpoints** - These include assessment of whether EYLEA prevents neovascular vision-threatening complications (such as progression to proliferative diabetic retinopathy (PDR) and anterior segment neovascularization) or progression to DME, as well as its impact on other anatomic effects, visual acuity improvement, and safety. Some secondary endpoints will be measured for up to two years.

Results from PANORAMA will be submitted for presentation at a future medical congress. PANORAMA will also form the basis of a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration later this year.

A separate ongoing trial sponsored by the Diabetic Retinopathy Clinical Research Network known as Protocol W is also evaluating EYLEA for the treatment of NPDR in patients without DME.

The safety and efficacy of the potential use of EYLEA in moderately severe to severe NPDR in patients without DME have not been fully evaluated by any regulatory authority.

About Diabetic Retinopathy
Approximately eight million people live with diabetic retinopathy, a 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 starts as NPDR and generally has no warning signs or symptoms. Approximately 560,000 people live with moderately severe to severe NPDR without DME in the U.S. As NPDR becomes more severe, DME can occur as the blood vessels in the retina become increasingly fragile and leak fluid, potentially causing visual impairment. NPDR may also progress to PDR, a stage of the disease in which abnormal blood vessels grow onto the surface of the retina and potentially cause severe, vision-threatening complications such as vitreous hemorrhage and traction retinal detachment.

About EYLEA® (aflibercept) Injection
EYLEA® (aflibercept) Injection is a vascular endothelial growth factor (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. In the U.S., EYLEA is the market-leading, FDA-approved anti-VEGF treatment for its approved indications and is supported by a robust body of research that includes seven pivotal Phase 3 trials.

IMPORTANT SAFETY INFORMATION FOR EYLEA® (aflibercept) INJECTION
EYLEA® (aflibercept) Injection is a prescription medication 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.

Injection into the eye with EYLEA can result in an infection in the eye and retinal detachment (separation of retina from back of the eye). 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 risk of serious and sometimes fatal side effects related to blood clots, leading to heart attack or stroke in patients receiving EYLEA.

Serious side effects related to the injection procedure with EYLEA are rare but can occur including infection inside the eye and retinal detachment.

The most common side effects reported in patients receiving EYLEA are increased redness in the eye, eye pain, cataract, moving spots in the field of vision, increased pressure in the eye, and vitreous (gel-like substance) detachment.

It is important that you 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.

EYLEA is for prescription use only. 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 is a prescription medicine approved for the treatment of patients with:

Wet Age-related Macular Degeneration (AMD): The recommended dose for EYLEA is 2 mg administered by injection in the eye every 2 months (8 weeks) following 3 initial monthly (every 4 weeks) injections. EYLEA may be dosed once per month, but in most patients, additional benefit was not seen with this dosing plan. Some patients may need monthly (every 4 weeks) dosing after the first 3 months (12 weeks).

Macular Edema following Retinal Vein Occlusion (RVO): The recommended dose for EYLEA is 2 mg administered by injection in the eye monthly (every 4 weeks).

Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR) in patients with DME: The recommended dose for EYLEA is 2 mg administered by injection in the eye every 2 months (8 weeks) following 5 initial monthly (every 4 weeks) injections. EYLEA may be dosed once per month, but in most patients, additional benefit was not seen with this dosing plan. Some patients may need monthly (every 4 weeks) dosing after the first 5 months (20 weeks).

Please visit www.EYLEA.us to see the full Prescribing Information for EYLEA.

The information contained herein is provided for general educational purposes. If you have any questions, talk to your doctor.

About Regeneron Pharmaceuticals, Inc.
Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to six FDA-approved treatments and numerous product candidates in development, all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye disease, heart disease, allergic and inflammatory diseases, pain, cancer, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*® technologies, such as *VelocImmune*® which produces optimized fully-human antibodies, and ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world.

For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

Forward-Looking Statements and Use of Digital Media
This news 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 Regeneron's products, 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 late-stage product candidates and new indications for marketed products, such any potential regulatory approval of EYLEA for moderately severe to severe non-proliferative diabetic retinopathy (including any potential approval by the U.S. Food and Drug Administration based on the planned supplemental Biologics License Application referenced in this news release); the extent to which the results from the research and development programs conducted by Regeneron or its collaborators (including the 24-week primary endpoint results from the Phase 3 PANORAMA trial reported in this news release) may be replicated in the future and lead to therapeutic applications; unforeseen safety issues and possible liability resulting from the administration of products and product candidates in patients, including without limitation EYLEA; serious complications or side effects in connection with the use of Regeneron's products and product candidates in clinical trials, such as the Phase 3 PANORAMA trial discussed in this news release; coverage and reimbursement determinations by third-party payers, including Medicare, Medicaid, and pharmacy benefit management companies; ongoing regulatory obligations and oversight impacting Regeneron's marketed products, research and clinical programs, and business, including those relating to the enrollment, completion, and meeting of the relevant endpoints of post-approval studies; 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 product candidates, such as EYLEA; competing drugs and product candidates that may be superior to Regeneron's products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's products and product candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on the commercial success of Regeneron's products and product candidates; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its sales or other 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, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), to be cancelled or terminated without any further product success; and risks associated with intellectual property of other parties and pending or future litigation relating thereto, including without limitation the patent litigation proceedings relating to Praluent® (alirocumab) Injection, the ultimate outcome of any such litigation proceedings, 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 United States Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2017. 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 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).

Contacts Regeneron:

Media Relations
Sarah Cornhill
Tel: +1 (917) 297-1522
sarah.cornhill@regeneron.com

Investor Relations
Manisha Narasimhan, Ph.D.
Tel: +1 (914) 847-5126
manisha.narasimhan@regeneron.com