Aflibercept 8 mg and EYLEA® (aflibercept) Injection Presentations at ARVO Provide New Insights into the Treatment of Serious Retinal Diseases

April 17, 2023

New subgroup data and further analyses of the aflibercept 8 mg clinical trial program to highlight durability results of extended dosing intervals, patient characteristics, and efficacy and safety in wet age-related macular degeneration and diabetic macular edema

18 presentations reinforce Regeneron's commitment to patients with serious retinal diseases

TARRYTOWN, N.Y., April 17, 2023 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) and its collaborator Bayer today announced that aflibercept 8 mg and EYLEA® (aflibercept) Injection will be featured in 18 presentations at the Association for Research in Vision and Ophthalmology (ARVO) 2023 Annual Meeting from April 23-27. Among the presentations will be new subgroup data and further analyses of aflibercept 8 mg treatment from the pivotal PULSAR and PHOTON trials in wet age-related macular degeneration (wAMD) and diabetic macular edema (DME), as well as the Phase 2 CANDELA trial in wAMD.

"Our data presentations at ARVO build on the more than 20 years of industry-leading knowledge and dedicated research aimed at addressing the unmet needs of patients with serious retinal diseases," said Boaz Hirshberg, M.D., Senior Vice President, Clinical Sciences General Medicine at Regeneron. "We look forward to sharing presentations on the efficacy and safety of EYLEA in multiple retinal diseases, as well as additional analyses of the pivotal aflibercept 8 mg trials – all of which reinforce our unwavering commitment to advancing retinal care for patients at risk of losing their vision."

Notable podium presentations will highlight the pivotal aflibercept 8 mg trials PULSAR and PHOTON, respectively, in wAMD and DME with 48-week efficacy and safety results, in addition to an evaluation of baseline characteristics of patients randomized to aflibercept 8 mg who maintained their dosing intervals and those whose dosing intervals were shortened. A pooled safety analysis of aflibercept 8 mg across the PULSAR, PHOTON and CANDELA trials will also be presented.

Data from PHOTON and PULSAR were first presented at the American Academy of Ophthalmology's annual meeting in September 2022. In February 2023, the U.S. Food and Drug Administration (FDA) accepted for Priority Review the Biologics License Application (BLA) for aflibercept 8 mg for treatment of patients with wAMD, DME and diabetic retinopathy with a target action date of June 27, 2023. Aflibercept 8 mg is investigational, and its safety and efficacy have not been fully evaluated by any regulatory authority.

Aflibercept 8 mg is being jointly developed by Regeneron and Bayer AG. In the U.S., Regeneron maintains exclusive rights to EYLEA and aflibercept 8 mg. Bayer has licensed the exclusive marketing rights outside of the U.S., where the companies share equally the profits from sales of EYLEA and future sales of aflibercept 8 mg following any regulatory approvals.

Aflibercept 8 mg and EYLEA presentations at ARVO:

Abstract title	Abstract	Lead author	Presentation date, time (CT), location
Aflibercept 8 mg			
Aflibercept 8 mg for diabetic macular edema: 48-week results from the Phase 2/3 PHOTON trial	#2814 Podium Presentation	Diana V. Do, M.D.	Tuesday, April 25 12:30 – 12:45 PM La Nouvelle AB
Intravitreal aflibercept 8 mg injection in patients with neovascular age-related macular degeneration: 48-week results from the Phase 3 PULSAR trial*	#461 Podium Presentation	Martin S. Spitzer, M.D.	Sunday, April 23 12:15 – 12:30 PM La Nouvelle AB
Baseline disease characteristics of patients who maintained 12- and 16-week aflibercept 8 mg dosing versus patients with shortened treatment intervals through week 48 in the Phase 2/3 PHOTON trial	#2813 Podium Presentation	David M. Brown, M.D., FACS	Tuesday, April 25 12:15 – 12:30 PM La Nouvelle AB
Baseline disease characteristics in patients maintaining q12 and q16 dosing with aflibercept 8 mg versus patients with shortened treatment intervals: A Phase 3 PULSAR post hoc analysis*	#2239 Poster Presentation	Paolo Lanzetta, M.D.	Monday, April 24 3:15 – 5:00 PM C0192
Pooled safety analysis of aflibercept 8 mg in the CANDELA, PHOTON, and PULSAR trials	#3724 Poster Presentation	Eric Schneider, M.D.	Tuesday, April 25 3:30 – 5:15 PM

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Additional visual and anatomic outcomes of intravitreal aflibercept injection 8 mg versus 2 mg: A post hoc analysis of the Phase 2 CANDELA study	#2180 Poster Presentation	Jordana G. Fein, M.D., M.S.	Monday, April 24 3:15 – 5:00 PM C0133
Intravitreal aflibercept 8 mg for diabetic macular edema: Week 48 efficacy outcomes by baseline demographics in the Phase 2/3 PHOTON trial	#2707 Poster Presentation	Ghassan Ghorayeb, M.D.	Tuesday, April 25 8:45 – 10:30 AM B0529
Subgroup analyses from the Phase 3 PULSAR trial of aflibercept 8 mg in patients with treatment-naïve neovascular age-related macular degeneration*	#2238 Poster Presentation	Sobha Sivaprasad, M.D.	Monday, April 24 3:15 – 5:00 PM C0191
Tolerability and safety of intravitreal aflibercept 8 mg in the Phase 3 PULSAR trial of patients with neovascular age-related macular degeneration*	#278 Poster Presentation	Jean-François Korobelnik, M.D., Ph.D.	Sunday, April 23 8:00 – 9:45 AM C0115
Intravitreal aflibercept 8 mg in patients with polypoidal choroidal vasculopathy (PCV): A Phase 3 PULSAR trial subgroup analysis*	#2240 Poster Presentation	Tien Y. Wong, M.D.	Monday, April 24 3:15 – 5:00 PM C0193
EYLEA			
Efficacy of intravitreal aflibercept versus laser photocoagulation for retinopathy of prematurity: Results from the Phase 3 BUTTERFLEYE trial	#5126 Podium Presentation	Darius M. Moshfeghi, M.D.	Thursday, April 27 11:30 – 11:45 AM 353-355
Impact of initial monthly doses of aflibercept on visual outcomes in eyes with diabetic macular edema in routine clinical practice in the US	#3646 Poster Presentation	Nitish Mehta, M.D.	Tuesday, April 25 3:30 – 5:15 PM C0423
Impact of baseline vision on visual outcomes and vision-related functions in eyes with diabetic macular edema: A post hoc analysis of VISTA and VIVID trials	#2703 Poster Presentation	Mark Barakat, M.D.	Tuesday, April 25 8:45 – 10:30 AM B0525
Intravitreal aflibercept in routine clinical practice: 24-month results from the global treatment-naïve cohort with macular edema secondary to central retinal vein occlusion in the AURIGA study*	#1762 Poster Presentation	Audrey Giocanti-Aurégan, M.D., Ph.D.	Monday, April 24 11:30 AM – 1:15 PM C0221
Intravitreal aflibercept in routine clinical practice: 24-month results from the global cohort of pretreated patients with diabetic macular edema in the AURIGA study*	#2637 Poster Presentation	Simone Donati, M.D.	Tuesday, April 25 8:45 – 10:30 AM B0459
Two-year results from a global observational study investigating proactive dosing regimens with intravitreal aflibercept in neovascular age-related macular degeneration (nAMD) in routine clinical practice: The XTEND study*	#462 Podium Presentation	Clare C. Bailey, M.D.	Sunday, April 23 12:30 – 12:45 PM La Nouvelle AB
Is there more to intravitreal aflibercept than anti-angiogenesis? Evaluating additional effects in DME through an *in silico* approach*	#2701 Poster Presentation	Ricardo P. Casaroli-Marano, M.D., M.Sc., Ph.D.	Tuesday, April 25 8:45 – 10:30 AM B0523
A post hoc analysis of intravitreal aflibercept–treated patients from ARIES & ALTAIR applying treatment regimen criteria from TENAYA & LUCERNE*	#2223 Poster Presentation	Michael Stewart, M.D.	Monday, April 24 3:15 – 5:00 PM C0176

**Bayer-run trial*

About the Aflibercept 8 mg 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: aflibercept 8 mg every 12 weeks, aflibercept 8 mg 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 aflibercept 8 mg in both trials had 3 initial monthly doses, and patients treated with EYLEA received 5 initial monthly doses in PHOTON and 3 in PULSAR. In the first year, patients in the aflibercept 8 mg 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, with those results still to be assessed. Patients in all EYLEA groups maintained a fixed 8-week dosing regimen throughout their participation in the trials.

CANDELA was a Phase 2 trial investigating the safety and efficacy of aflibercept 8 mg extended dosing regimens compared to EYLEA in wAMD patients.

About wAMD and DME
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 1.1 million Americans have wAMD, and this number is expected to double by 2050.

DME is a common complication in eyes of people living with diabetes. DME occurs when high levels of blood sugar lead to damaged blood vessels in the eye that leak fluid into the macula. This can lead to vision loss and, in some cases, blindness. Of the nearly 28 million American adults living with diabetes, an estimated 1.2 million have 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 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 EYLEA SAFETY INFORMATION AND INDICATIONS

INDICATIONS
EYLEA (aflibercept) Injection 2 mg (0.05 mL) is indicated for the treatment of patients with Neovascular (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 [0.01 mL]).

CONTRAINDICATIONS

- EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

WARNINGS AND PRECAUTIONS

- Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients and/or caregivers should be instructed to report any signs and/or symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.
- Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.
- In infants with ROP, reactivation of abnormal angiogenesis and tortuosity may occur following treatment with EYLEA. Infants should be monitored closely after injection with EYLEA until retinal vascularization has completed or until the examiner is assured that reactivation of ROP will not occur. Treatment with EYLEA will necessitate extended periods of ROP monitoring and additional EYLEA injections and/or laser treatments may be necessary.
- There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

ADVERSE REACTIONS

- Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.
- The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.
- In pre-term infants with ROP receiving EYLEA the most common adverse reactions (≥4%) reported were retinal detachment, conjunctival hemorrhage, and intraocular pressure increased. Adverse reactions established for adult indications are considered applicable to pre-term infants with ROP, though not all were observed in the clinical studies.
- Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

For more information, please see full Prescribing Information.

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 nearly 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 aflibercept 8 mg and EYLEA® (aflibercept) Injection; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates and new indications for Regeneron's Products, such as aflibercept 8 mg for the treatment of patients with wet age-related macular degeneration, diabetic macular edema, and diabetic retinopathy (including potential approval by the U.S. Food and Drug Administration based on the Biologics License Application referenced in this press release); 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 or any potential regulatory approval of Regeneron's Products and Regeneron's Product Candidates (such as aflibercept 8 mg); 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 (such as aflibercept 8 mg) 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 aflibercept 8 mg and 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 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, 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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