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News Release

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Aflibercept 8 mg clinical study data now published in *The Lancet*

- Aflibercept 8 mg (Eylea™ 8 mg) with extended treatment intervals of 12 or 16 weeks demonstrated non-inferior vision gains versus standard of care aflibercept 2 mg (Eylea™ 2 mg) at fixed 8-week dosing for patients with neovascular (wet) age-related macular degeneration (nAMD) and diabetic macular edema (DME) in the first year (at week 48)
- Eylea 8 mg is the first drug to show unprecedented durability results, rapid and resilient fluid control, and a safety profile comparable to standard of care Eylea 2 mg
- Extended dosing intervals with Eylea 8 mg have the potential to substantially reduce treatment burden and improve patient management for healthcare professionals in ophthalmology

Berlin, March 8, 2024 – *The Lancet* has published clinical trial data for aflibercept 8 mg (Eylea™ 8 mg) from the pivotal phase III PULSAR study in neovascular (wet) age-related macular degeneration (nAMD) and phase II/III PHOTON study in diabetic macular edema (DME) in the first year of treatment (at week 48).

Both studies met their primary endpoint of non-inferior best corrected visual acuity (BCVA) changes with two extended dosing intervals (every 12 or 16 weeks) of Eylea 8 mg compared to standard of care Eylea 2 mg with a fixed 8-week dosing interval, following initial monthly doses. Eylea 8 mg demonstrated unprecedented durability results in the vast majority of patients: 77% of nAMD patients and 89% of DME patients maintained 16-week dosing intervals with Eylea 8 mg with an average of 5 injections (versus 7-8 injections with Eylea 2 mg with a fixed 8-week dosing interval) through week 48. In the 12-week dosing group, 79% of nAMD patients and 91% of DME patients maintained this dosing interval with Eylea 8 mg with an average of 6 injections through week 48. The safety profile of Eylea 8 mg was consistent with that of Eylea 2 mg.

“In its clinical trials, Eylea 8 mg has shown meaningful and clinically relevant benefits, enabling patients to achieve sustained disease control. This means uniquely delivering lasting vision gains with extended treatment intervals, rapid and resilient fluid control, and a safety profile comparable to Eylea 2 mg,” said Prof. Paolo Lanzetta, Chairman of the Department of Ophthalmology at the University of Udine, Italy, and a member of the steering committee of the clinical trials.

“Non-adherence and non-persistence remain a significant challenge for patients with retinal diseases due to a need for frequent injections and visits to eye clinics. Eylea 8 mg has the potential to reduce that disease burden by extending treatment intervals. This may contribute to improved adherence and persistence and ultimately improve patient outcomes” said Sobha Sivaprasad, Professor and Consultant Ophthalmologist, Moorfields Eye Hospital, London, UK, and member of the steering committee of the PHOTON study.

PULSAR and PHOTON are the first randomised controlled clinical trials comparing Eylea 8 mg to the standard of care Eylea 2 mg in nAMD and DME

The results from PULSAR and PHOTON, outlined in *The Lancet,* provide strong evidence of the comparable visual and anatomic outcomes of Eylea 8 mg administered at extended dosing intervals to Eylea 2 mg through 48 weeks.

In both studies, Eylea 8 mg (12- and 16-week groups) demonstrated comparable outcomes in the primary efficacy endpoint of change from baseline in best corrected visual acuity (BCVA) at week 48 to the standard of care Eylea 2 mg (every 8 weeks). PULSAR adjusted means: +6.1 and +5.9 letter gains with Eylea 8 mg 12- and 16-week group versus +7.0 letters with Eylea 2 mg; in PHOTON adjusted means: +8.1 and +7.2 letter gains with Eylea 8 mg 12- and 16-week group versus +8.7 letters with Eylea 2 mg.

In addition to vision, anatomic outcomes were evaluated as secondary endpoints in both studies. In PULSAR, the Eylea 8 mg combined group demonstrated statistically significant superior fluid control with 63% of patients with no retinal fluid in the central subfield versus 52% in the Eylea 2 mg group at week 16. Robust fluid control was maintained through to week 48.

In PHOTON, similar reductions in mean change from baseline of central retinal thickness (CRT) at week 48 were achieved in DME patients receiving Eylea 8 mg with 12- and 16-week dosing versus Eylea 2 mg.

In both studies, the safety profile of Eylea 8 mg was shown to be consistent with that of Eylea 2 mg. The number of patients with intraocular inflammation (IOI) was low across all treatment groups, and no cases of endophthalmitis or retinal vasculitis were reported. There was no difference in intraocular pressure increase rates compared to Eylea 2 mg.

The lead sponsors of the trials were Bayer for PULSAR and Regeneron for PHOTON.

Eylea HD (aflibercept 8 mg) has been approved for use by the FDA in August 2023. To date, Eylea™ 8 mg (aflibercept 8 mg, 114.3 mg/ml solution for injection) has been approved in the EU, Japan, and other markets for the treatment of nAMD and DME. Bayer has submitted regulatory applications for aflibercept 8 mg in additional markets.

Eylea 8 mg (aflibercept 8 mg; in the United States: Eylea HD) is being jointly developed by Bayer and Regeneron. Regeneron maintains exclusive rights to Eylea 2 mg (aflibercept 2 mg) and Eylea HD 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 2 mg and Eylea 8 mg following any regulatory approvals.

About PULSAR and PHOTON

PULSAR and PHOTON are randomized, double-masked, active-controlled pivotal trials. Both trials were conducted in multiple centers globally with similar designs and endpoints. The Phase III PULSAR trial in nAMD and Phase II/III PHOTON trial in DME evaluated the efficacy and safety of aflibercept 8 mg with 12- and 16-week dosing regimens versus Eylea (aflibercept 2 mg) dosed every 8 weeks, following initial monthly doses, with the primary endpoint of non-inferiority in terms of best corrected visual acuity (BCVA) at week 48. The two-year data mark the end of the masked study (week 96) with the option to extend treatment intervals up to 24 weeks and with an optional 1-year open-label extension for patients until week 156. Patients in both clinical trials were randomized at baseline to the three different arms. Across both studies, 1,164 patients were treated with aflibercept 8 mg. All patients in the aflibercept 8 mg arms were continuously evaluated under stringent, clinically relevant, patient focused dose regimen modification (DRM) criteria starting from week 16 throughout the studies. 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 DRM criteria for disease progression were observed. Intervals could not be extended until the second year of the studies. In the second year, patients in the aflibercept 8 mg groups could have their dosing intervals shortened or extended if DRM criteria were met. Patients in all Eylea (aflibercept 2 mg) groups maintained a fixed 8-week dosing regimen throughout their participation in the trials. The lead sponsors of the trials were Bayer for PULSAR and Regeneron for PHOTON.

About nAMD and DME

Neovascular (wet) age-related macular degeneration (nAMD) is an eye disease that progresses rapidly and if left untreated can lead to vision loss in a few months. nAMD is one of the leading causes of irreversible blindness and vision impairment around the world. nAMD 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. 196 million people worldwide are living with AMD – it is anticipated that this figure will increase to 288 million by 2040. Approximately 10-15% of people with AMD will develop the advanced form nAMD.

Diabetic macular edema (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. Globally, 146 million people are currently living with diabetic retinopathy (DR), which can develop into a more serious condition which is diabetic macular edema. DME is affecting around 21 million people globally.

About Bayer

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around 100,000 people and had sales of 47.6 billion euros. R&D expenses before special items amounted to 5.8 billion euros. For more information, go to www.bayer.com.

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Forward-Looking Statements
This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.