Aflibercept 8 mg late-breaking data at the 55th Annual Scientific Meeting 2022 of the Retina Society:

Detailed data from pivotal studies with aflibercept 8 mg demonstrate sustained improvements in visual acuity and anatomic measures with large majority of patients maintaining treatment intervals of 16 weeks at week 48

- Aflibercept 8 mg maintained 16-week dosing intervals in up to 89% of patients with as few as 5 injections until week 48
- Aflibercept 8 mg demonstrated non-inferior vision gains to Eylea® (aflibercept 2 mg) with 83% of patients with neovascular (wet) age-related macular degeneration (nAMD) and 93% of patients with diabetic macular edema (DME) maintaining dosing intervals of 12 weeks or longer through week 48
- Superior fluid control in nAMD and robust disease control through to week 48 in nAMD and DME
- In both studies, similar reductions in mean change of central retinal thickness (CRT) were achieved in patients receiving aflibercept 8 mg with 12- and 16-week dosing versus Eylea with 8-week dosing at week 48
- Safety of aflibercept 8 mg was consistent with the well-established safety profile of Eylea

Berlin, November 5, 2022 – Bayer AG today announced that detailed results from two pivotal clinical studies have demonstrated sustained visual acuity and anatomic improvements with aflibercept 8 mg with 12- and 16-week dosing regimens versus Eylea® (aflibercept 2 mg) with 8-week dosing at week 48.

The phase III PULSAR trial in neovascular (wet) age-related macular degeneration (nAMD) and phase II/III PHOTON trial in diabetic macular edema (DME) respectively met their primary endpoint of non-inferiority of aflibercept 8 mg extended dosing regimens for
best corrected visual acuity (BCVA) at week 48, compared to Eylea dosed every 8 weeks, all following initial monthly doses. Patients were randomized in three different arms and all patients in the aflibercept 8 mg arms were continuously evaluated under stringent, clinically relevant, and patient focused dosing regimen modification (DRM) criteria. 77% of nAMD and 89% of DME patients maintained every 16-week dosing intervals with aflibercept 8 mg at week 48 in the clinical trials.

In the pooled data-analysis, aflibercept 8 mg demonstrated sustained visual acuity with 83% of nAMD patients and 93% of DME patients, maintaining dosing intervals of 12 weeks or longer through week 48.

The full study results were presented during two late-breaking sessions at the 55th Annual Scientific Meeting of the Retina Society, USA. Bayer will submit these data to regulatory authorities outside of the USA.

“These data show unprecedented durability of aflibercept 8 mg in patients living with age-related macular degeneration and diabetic macular edema, who also experienced significant anatomical improvements at week 48,” said Jean-François Korobelnik, Professor of Ophthalmology and Head of the Department of Ophthalmology at University Hospital of Bordeaux in France and a principal trial investigator.

“As Eylea is a high impact therapy based on scientific innovation – an amazing story and remains the global standard of care for age-related macular degeneration and diabetic macular edema and the evidence for aflibercept 8 mg can support us in further relieving the burden for patients and healthcare providers,” said Dr. Christian Rommel, Member of the Executive Committee of Bayer’s Pharmaceutical Division and Head of Research and Development. “As a potential new treatment, aflibercept 8 mg offers the possibility of extended treatment intervals without compromising on efficacy and safety. We look forward to working with regulatory authorities to make aflibercept 8 mg available.”

As presented at the Retina Society, in the PULSAR trial in nAMD, the observed arithmetic mean change from baseline in BCVA at week 48 was +6.7 letters in the aflibercept 8 mg arm under a 12-week injection interval and +6.2 letters in the aflibercept 8 mg arm under a 16-week injection interval versus +7.6 letters in the Eylea arm under 8-week injection interval. For patients in the aflibercept 8 mg arm under the 16-week dosing schedule, the mean number of injections to week 48 was reduced to 5.2, and under the 12-week dosing schedule 6.1 injections, compared with 6.9 in the Eylea arm on an 8-week dosing
schedule. The proportion of patients with BCVA letter score gains (measured by the ETDRS letter score) at week 48 was comparable among the treatment groups.

PULSAR also met its key secondary endpoint, demonstrating superiority of aflibercept 8 mg in improving anatomic outcomes of retinal fluid at week 16 versus Eylea (p=0.0002) which was maintained through week 48. Notably, 71% and 67% of aflibercept 8 mg nAMD patients in the 12- and 16-week dosing arms had no retinal fluid in the center subfield, compared to 59% for Eylea with 8-week dosing at week 48. The median time to a fluid-free center subfield in the aflibercept 8 mg 12- and 16-week arms were 4 weeks versus 8 weeks in the Eylea arm. Similar reductions in mean change of central retinal thickness (CRT) from baseline were achieved in patients receiving aflibercept 8 mg 12- and 16-week dosing versus Eylea with 8-week dosing at week 48.

In the PHOTON trial in DME, the observed arithmetic mean change from baseline in BCVA at week 48 was +8.8 letters in the aflibercept 8 mg arm under a 12-week injection interval and +7.9 letters in the aflibercept 8 mg arm under a 16-week injection interval versus +9.2 letters in the Eylea arm with every 8-week injection interval. Until week 48, patients in the aflibercept 8 mg arm on a 16-week dosing schedule received a mean number of 4.9 injections and 5.7 injections on a 12-week dosing schedule, compared to 7.7 injections in the Eylea arm under an 8-week dosing schedule. Among DME patients, there was a mean reduction of 14 mm² (n= 328) and 9 mm² (n=136) in the total area of fluorescein leakage from baseline for aflibercept 8 mg on 12-week and 16-week dosing groups, respectively, compared to 9 mm² for Eylea (n=167), per an exploratory analysis of PHOTON. Reductions in fluorescein leakage, a measure of disease activity, are associated with disease improvement. Similar reductions in mean change from baseline of central retinal thickness (CRT) at week 48 were achieved in DME patients receiving aflibercept 8 mg with 12- and 16-week dosing versus Eylea with 8-week dosing.

The safety of aflibercept 8 mg was consistent with the well-established safety profile of Eylea. Pre-injection intraocular pressure (IOP) values were similar to baseline values at all timepoints through week 48. Patients with IOP ≥ 35 mmHg pre- or post-injection at any timepoint for aflibercept 8 mg versus Eylea were 0.6% versus 0.3% in PULSAR and 0.2% versus 1.2% in PHOTON. The rates of intraocular inflammation for aflibercept 8 mg versus Eylea were 0.7% versus 0.6% in PULSAR and 0.8% versus 0.6% in PHOTON at week 48. Furthermore, there were no cases of occlusive retinal vasculitis or
endophthalmitis in either trial, and non-ocular events were balanced between all treatment groups with no new signals.

Data from PULSAR and PHOTON were first shared in September 2022 and first presented at the American Association for Ophthalmology Annual Meeting.

Aflibercept 8 mg is being jointly developed by Bayer and Regeneron. Regeneron maintains exclusive rights to Eylea and aflibercept 8 mg 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.

Aflibercept 8 mg is investigational, and its safety and efficacy have not yet been evaluated by any regulatory authority.

About trial design of PULSAR and PHOTON
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 (8q12, 8q16) versus Eylea (aflibercept 2 mg) dosed every 8 weeks (2q8) with the primary endpoint at week 48. Patients in both clinical trials were randomized and assigned to the three different arms (8q12, 8q16, 2q8). All patients in the aflibercept 8 mg arms were continuously evaluated under stringent, clinically relevant, patient focused dosing regimen modification (DRM) criteria starting from week 16. If patients on 8q12 or 8q16 met DRM criteria at week 16 or 20, treatment interval was shortened to 2q8. If patients on 8q16 met DRM criteria at week 24, treatment interval was shortened to 8q12. If patients on aflibercept 8 mg arms met the DRM criteria in any following dosing visits, the treatment interval was further shortened, with a minimum interval of 8 weeks. For patients whose treatment interval was shortened, no extension was allowed in year 1. The DRM criteria in PULSAR were: >5-letter loss in BCVA due to persistent or worsening nAMD and >25 µm increase in CRT compared to week 12 or new onset of foveal neovascularization or foveal hemorrhage. The DRM criteria in PHOTON were: >10-letter loss in BCVA due to persistent or worsening DME and >50 µm increase in CRT compared to week 12.

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 as little as three 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.

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).

About Bayer
Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. Its products and services are designed to help people and the planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. Bayer is committed to driving sustainable development and generating a positive impact with its businesses. At the same time, the Group aims to increase its earning power and create value through innovation and growth. The Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2021, the Group employed around 100,000 people and had sales of 44.1 billion euros. R&D expenses before special items amounted to 5.3 billion euros. For more information, go to www.bayer.com.

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1 ETDRS, Early treatment of diabetic retinopathy study