News Release

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American College of Cardiology's 71st Annual Scientific Session (ACC.22):

Bayer presents positive results from first Phase 2b trial on safety of asundexian in patients with atrial fibrillation

- Data from the PACIFIC-AF trial demonstrated lower observed rates of ISTH major and clinically relevant non-major bleeding for asundexian (a FXIa inhibitor) compared with apixaban in patients with atrial fibrillation at risk of stroke
- The data, simultaneously published today in The Lancet, found that both 20 mg and 50 mg doses of asundexian were well-tolerated and resulted in significantly lower rates of bleeding compared with apixaban while achieving almost complete inhibition of FXIa
- This trial was designed as a dose-finding phase 2 clinical study. It was not powered to discern or test differences in the rates of thrombotic events.

Berlin, April 3, 2022 – Bayer today announced positive data from the PACFIC-AF trial which compared the safety of the investigational, oral Factor XIa (FXIa) inhibitor asundexian with apixaban (a non-vitamin K antagonist oral anticoagulant) in patients with atrial fibrillation (AF). The results found that the bleeding rate for the primary endpoint (ISTH major and clinically relevant non-major bleeding) was reduced by 67% (incidence proportion of 0.33*) in patients receiving asundexian compared to those receiving apixaban. By selectively modulating coagulation, once-daily FXIa inhibitor asundexian is being investigated to become a new treatment option in thrombosis prevention. The findings were presented today at the American College of Cardiology's 71st Annual Scientific Session (ACC.22), and simultaneously published in *The Lancet*.

* A 67% reduction in the bleeding rate corresponds to an incidence proportion of 0.33 when comparing the pooled asundexian doses with apixaban

“There is an unmet need for stroke prevention in people with atrial fibrillation,” said Manesh Patel, Richard S. Stack Distinguished Professor, Chief of the Division of Cardiology and Co-Director of the Heart Center at Duke University. “Despite guidelines recommending oral anticoagulation treatment of patients with atrial fibrillation, around 40% of AF patients are either under-treated, receiving a lower dose than is recommended, or not treated at all. This can leave patients vulnerable to potentially life-changing thrombo-embolic events, such as stroke.” He continued, “The PACIFIC-AF data showed asundexian had significantly less bleeding compared to apixaban in AF patients at risk of stroke, while achieving near complete FXIa inhibition levels. As we embark on approval studies, this potential new therapy would mark a much-welcomed advance in patient care.”

PACIFIC-AF is the first head-to-head trial to compare the bleeding risk of an oral FXIa inhibitor vs. a non-vitamin K antagonist oral anticoagulant (NOAC) in patients with AF who are at risk of stroke. The trial’s primary objective was to determine whether treatment with asundexian can lead to a lower incidence of ISTH major and clinically relevant non-major bleeding when compared with apixaban in patients with AF. It also aimed to determine the optimal dose of asundexian, 20 mg or 50 mg once-daily, in these patients. This trial was not powered to discern or test differences in the rates of thrombotic events.

“Today’s clinical research findings provide additional support for the mechanism and safety profile of asundexian in patients with AF,” said Dr. Christian Rommel, Member of the Executive Committee of Bayer AG's Pharmaceutical Division and Head of Research and Development at Bayer. “With our FXI(a) inhibitor program, Bayer is developing innovative, next-generation therapies for patients and families impacted by cardiovascular disease.”

About the PACIFIC-AF Trial

PACIFIC-AF was a randomized, double-blind Phase 2 dose-finding study, comparing asundexian 20 mg or 50 mg once-daily with apixaban twice daily in patients with AF and a CHA_2DS_2-VASc score ≥2 if male or ≥3 if female, with increased bleeding risk. The primary endpoint was the composite of major or clinically relevant non-major bleeding. The trial included 755 patients, with a mean age of 73.7 years. Asundexian 20 mg and 50 mg resulted in 81–90% and 92–94% inhibition of FXIa activity at trough and peak concentrations of asundexian, respectively. At both 20 mg and 50 mg doses, asundexian

resulted in significantly lower rates of bleeding compared with apixaban (incidence proportion of 0.33 for pooled doses), with near complete in-vivo FXIa inhibition.

About Asundexian and FXIa Inhibitors

By specifically targeting a protein involved in pathological thrombus formation but leaving the pathway involved in physiological vessel healing intact, asundexian (BAY2433334) could have the potential to prevent thrombo-embolic events without a corresponding increase in bleeding risk. Its mechanism of action could represent a new treatment option in thrombosis prevention. The PACIFIC clinical program is designed to provide further support for the hypothesis that inhibiting FXIa with asundexian can reduce the risk of thrombotic events such as stroke and myocardial infarction without increasing the risk of bleeding.

Asundexian is a once-daily, oral investigational agent and has not been approved by any health authority for use in any country, for any indication.

About the FXIa Clinical Trial Program

Asundexian is currently being studied in the PACIFIC Phase 2 clinical trial program that consists of three Phase 2b studies, each one focusing on one of the following medical conditions: atrial fibrillation (irregular heartbeat), a recent non-cardioembolic ischemic stroke or a recent acute myocardial infarction (heart attack). These trials form part of the broadest Phase 2b FXIa program in the world, involving more than 4,000 patients to date. The program continues the legacy of Bayer's rivaroxaban program, the largest and most extensive research program ever conducted in the thrombosis space and delivers on Bayer's commitment to address unmet needs in a growing range of underserved cardiovascular patient communities.

More information about these trials is available at http://www.clinicaltrials.gov/. The National Clinical Trial numbers for these studies are PACIFIC-AF (atrial fibrillation) NCT04218266, PACIFIC-STROKE (non-cardioembolic ischemic stroke) NCT04304508 and PACIFIC-AMI (myocardial infarction) NCT04304534.

About Atrial Fibrillation

AF is the most common sustained cardiac rhythm disorder. In AF, the upper chambers (atria) of the heart contract irregularly.[1] As a result, the atria do not empty completely, and

blood does not flow properly, potentially allowing blood clots to form. These blood clots can break loose and travel to the brain, resulting in a stroke.[2]

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 planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. Bayer is committed to drive sustainable development and generate 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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Forward-Looking Statements
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References

1. NHS choices. Atrial fibrillation. Available at: http://www.nhs.uk/Conditions/Atrial-fibrillation Accessed March 2022

2. NHS choices. Atrial fibrillation complications. Available at: http://www.nhs.uk/Conditions/Atrial-fibrillation/Pages/Complications.aspx Accessed March 2022