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News Release

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Data from Phase III VOYAGER PAD study published in *The New England Journal of Medicine* and presented during the American College of Cardiology's 69th Annual Scientific Session together with World Congress of Cardiology (ACC.20/WCC Virtual)

Xarelto™ 2.5 mg plus aspirin significantly lowered the combined risk of limb ischemia and major cardiovascular events in patients with symptomatic peripheral artery disease post revascularization

- The only clinical outcome study to demonstrate the benefits of a combined antithrombotic and anti-platelet therapy in these vulnerable patients who currently have limited treatment options
- Risk of acute limb ischemia was significantly reduced by 33% in these patients compared to those receiving aspirin alone
- There was no significant increase in TIMI major bleeding, the principal safety outcome of the trial

Berlin, March 28, 2020 – In the Phase III VOYAGER PAD study Bayer´s Factor Xa inhibitor Xarelto™ (rivaroxaban) met its primary efficacy endpoint. The study investigated Xarelto vascular dose, 2.5 mg twice daily, plus aspirin 100 mg once daily in comparison to aspirin alone. Results showed a significantly reduced risk of the composite outcome of acute limb ischemia (ALI), major amputation due to a vascular etiology, heart attack, ischemic stroke or cardiovascular death by 15% (relative risk reduction) in patients with symptomatic peripheral artery disease (PAD) up to 10 days after lower extremity revascularization procedures. These patients have a high risk of cardiovascular or limb events and until now have had limited treatment options. The risk of acute limb ischemia was significantly reduced by 33% in comparison to aspirin alone.

In the VOYAGER PAD study, the incidence rates of the principal safety outcome TIMI major bleeding were not significantly different between the treatment arms (TIMI: thrombolysis in myocardial infarction classification). Rates of the secondary safety outcome of ISTH major bleeding were higher with rivaroxaban 2,5 mg twice daily plus

aspirin than with aspirin alone. In addition to the results of the earlier COMPASS study, VOYAGER PAD provides further evidence that Xarelto vascular dose in combination with aspirin is protecting patients from atherothrombotic events. These data were presented as part of a Late-Breaking Clinical Trial Session during the virtual sessions of the American College of Cardiology's 69th Annual Scientific Session together with World Congress of Cardiology, 28 - 30 March and published simultaneously in *The New England Journal of Medicine*.

"In spite of current therapies, at least one in five patients with PAD undergoing revascularization will have acute limb ischemia, major amputation of vascular etiology, heart attack, ischemic stroke or cardiovascular death at three years," said Dr. Marc Bonaca, Director of Vascular Research at the University of Colorado, USA and a VOYAGER Executive Committee member. "The results of VOYAGER PAD demonstrate that the risk profile in this population and in this setting is dominated by acute limb ischemia and amputation in addition to major cardiovascular events, and that the combination of rivaroxaban 2.5 mg twice daily and low dose aspirin significantly reduces this risk. In addition, there are broad benefits for reducing key outcomes like the need for unplanned index limb revascularization. Key new information is the safety in this setting, and while there were higher rates of bleeding with rivaroxaban, there was net benefit and no excess in intracranial hemorrhage or fatal bleeding."

VOYAGER PAD is the only successful clinical outcome study to demonstrate the benefits of combined antithrombotic and anti-platelet therapy, showing a reduced risk of major limb events following peripheral revascularization. Importantly, the study demonstrated a 28% reduction in hospitalizations related to coronary or peripheral thrombotic events and a 12% reduction in further limb revascularizations in patients receiving Xarelto vascular dose, 2.5 mg twice daily plus aspirin 100 mg.

"The efficacy and safety of a dual pathway approach with Xarelto vascular dose and aspirin has been demonstrated in over 60,000 patients across a large spectrum of cardiovascular diseases," said Dr Joerg Moeller, Member of the Executive Committee of Bayer AG's Pharmaceutical Division and Head of Research and Development. "This study further differentiates Xarelto as the only NOAC that has demonstrated efficacy in combination with anti-platelet therapy in patients with peripheral artery disease."

PAD is caused by atherosclerosis, a chronic progressive disease, which is characterized by a build-up of plaque in the arteries limiting blood flow to the limbs. Approximately 202 million people globally are affected by PAD and those with the condition are also at a higher risk of having CAD and other vascular diseases.

About VOYAGER PAD

The Phase III VOYAGER PAD study included 6,564 patients from 534 sites across 34 countries worldwide. In the study, patients were randomized to receive either Xarelto vascular dose 2.5 mg twice daily plus aspirin 100 mg once daily or aspirin 100 mg once daily alone. The primary efficacy endpoint was a composite of acute limb ischemia (ALI), major amputation of a vascular etiology, heart attack (myocardial infarction, MI), ischemic stroke or cardiovascular death. The primary safety outcome was major bleeding according to the thrombolysis in myocardial infarction (TIMI) classification.

Efficacy Outcomes

For the primary efficacy outcome, Xarelto vascular dose 2.5 mg twice daily plus aspirin 100 mg once daily was superior to aspirin 100 mg once daily alone for the prevention of the composite endpoint of ALI, major amputation due to a vascular etiology, MI, ischemic stroke or cardiovascular death, (hazard ratio (HR) 0.85; 95% confidence interval (CI) 0.76-0.96; P=0.0043).

The results for the individual components are captured below:

- ALI: HR 0.67; 95% CI 0.55-0.82
- Major amputation due to a vascular etiology: HR 0.89; 95% CI 0.68-1.16
- MI: HR 0.88; 95% CI 0.70-1.12
- Ischemic stroke: HR 0.87; 95% CI 0.63-1.19
- CV death: HR 1.14; 95% CI 0.93-1.40.

Safety Outcomes

Rates of the principal safety outcome of TIMI major bleeding were not significantly different between groups (HR 1.43, 95% CI 0.97-2.10). There was no increase in fatal bleeding (HR 1.02; 95% CI 0.33-3.15) and a numerical decrease in intracranial bleeding (HR 0.78; 95% CI 0.38-1.61). The rate of the secondary safety outcome of ISTH major bleeding was statistically significantly higher with rivaroxaban 2.5 mg plus aspirin than with aspirin alone.

About Rivaroxaban (Xarelto™)

Rivaroxaban is the most broadly indicated non-vitamin K antagonist oral anticoagulant (NOAC) worldwide and is marketed under the brand name Xarelto. Xarelto is approved for more venous and arterial thromboembolic (VAT) conditions than any other NOAC:

- The prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF) and one or more risk factors
- The treatment of pulmonary embolism (PE) in adults
- The treatment of deep vein thrombosis (DVT) in adults
- The prevention of recurrent PE and/or DVT in adults
- The prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip replacement surgery
- The prevention of VTE in adult patients undergoing elective knee replacement surgery
- The prevention of atherothrombotic events after an Acute Coronary Syndrome in adult patients with elevated cardiac biomarkers when co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine
- The prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk for ischaemic events when co-administered with acetylsalicylic acid (ASA)

Whilst licences may differ from country to country, across all indications Xarelto is approved in more than 130 countries.

Rivaroxaban was discovered by Bayer, and is being jointly developed with Janssen Research & Development, LLC. Xarelto is marketed outside the U.S. by Bayer and in the U.S. by Janssen Pharmaceuticals, Inc. (Janssen Research & Development, LLC and Janssen Pharmaceuticals, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson).

Anticoagulant medicines are potent therapies used to prevent or treat serious illnesses and potentially life-threatening conditions. Before initiating and while continuing treatment with anticoagulant medicines, physicians should carefully assess the benefit and risk for the individual patient.

Responsible use of Xarelto is a very high priority for Bayer, and the company has developed a Prescribers Guide for physicians and a Xarelto Patient Card for patients to support best practice.

To learn more about thrombosis, please visit www.thrombosisadviser.com and www.vascularadviser.com

To learn more about Xarelto, please visit www.xarelto.com

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 benefit people by supporting efforts to overcome the major challenges presented by a growing and aging global population. At the same time, the Group aims to increase its earning power and create value through innovation and growth. Bayer is committed to the principles of sustainable development, and the Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2019, the Group employed around 104,000 people and had sales of 43.5 billion euros. Capital expenditures amounted to 2.9 billion euros, R&D expenses to 5.3 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.