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News Release

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Rivaroxaban application submitted to U.S. FDA for new indication in patients after lower-extremity revascularization due to symptomatic PAD

- FDA submission based on results from Phase III VOYAGER PAD study which showed a significant reduction in the primary efficacy endpoint in patients after lower-extremity revascularization due to symptomatic peripheral artery disease (PAD)
 - There is currently no Class I Guideline recommended treatment for this patient population
 - It is estimated that as many as 20 million Americans are living with PAD
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Berlin, October 26, 2020 – Bayer's development partner, Janssen Research & Development, LLC, has submitted a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for a new indication to expand the use of Xarelto™ (rivaroxaban) in people with peripheral artery disease (PAD) to include those after recent lower-extremity revascularization due to symptomatic PAD.

The application is based on data from the Phase III VOYAGER PAD trial. These data were presented during the American College of Cardiology's 69th Annual Scientific Session in March 2020 and published simultaneously in *The New England Journal of Medicine*. They showed that Xarelto vascular dose (2.5 mg twice daily) plus aspirin (100 mg once daily) was superior to aspirin alone in reducing the primary efficacy endpoint; a composite of acute limb ischemia, major amputation of a vascular etiology, heart attack, ischemic stroke or cardiovascular death, with similar rates of Thrombolysis in Myocardial Infarction (TIMI) major bleeding.

Two major Phase III trials - VOYAGER PAD and COMPASS - have now evaluated the use of dual antithrombotic pathway inhibition with Xarelto in combination with aspirin in more than 14,000 patients with PAD. Xarelto, in combination with aspirin, was approved by the FDA in 2018 to reduce the risk of major cardiovascular (CV) events in patients with

chronic PAD and coronary artery disease (CAD). It is the only direct oral anticoagulant (DOAC) approved for use in these patients. The VOYAGER PAD trial is the first to demonstrate the benefits of dual pathway inhibition in patients with symptomatic PAD post revascularization, for whom there are currently limited treatment options and no Class I Guideline recommended treatment.

“By demonstrating the efficacy of dual pathway inhibition in patients with PAD who have recently undergone a revascularization procedure, the VOYAGER PAD study results reinforce the benefits of Xarelto in patients with PAD,” said Dr Joerg Moeller, Member of the Executive Committee at Bayer AG’s Pharmaceuticals Division and Head of Research and Development.

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. It is a serious underlying health crisis that impacts an estimated 20 million Americans with only 8.5 million diagnosed. PAD increases the risk for major CV events and is the leading cause of amputation which can double a patient’s risk of death.

In Europe, Bayer had submitted a variation to include the VOYAGER PAD data in the label of Xarelto in August 2020. The treatment of patients with symptomatic PAD at high risk for ischaemic events is already approved for Xarelto when co-administered with aspirin. The VOYAGER PAD study proves the benefits of Xarelto in patients with symptomatic PAD after lower-extremity revascularization.

About the VOYAGER PAD study

The Phase III VOYAGER PAD study included 6,564 patients from 542 sites across 34 countries worldwide. In the study, patients were randomized to receive either Xarelto 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, 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.

About Xarelto™

Rivaroxaban is the most broadly indicated non-vitamin K antagonist oral anticoagulant (NOAC) and is marketed under the brand name Xarelto™. Xarelto is approved for eight

indications, protecting patients across 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) with 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 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 (cardiovascular (CV) death, myocardial infarction (MI) or stroke) after an acute coronary syndrome in adult patients with elevated cardiac biomarkers and no prior stroke or transient ischaemic attack (TIA) 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

Xarelto is approved in more than 130 countries, whilst the approved labeling, including the number of indications may differ from country to country.

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 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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