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News Release

Not intended for U.S. and UK Media

New study results add to solid evidence for the efficacy and safety of Rivaroxaban in the prevention of venous thromboembolism:

Rivaroxaban significantly reduced risk of major venous thromboembolism following nonmajor orthopaedic surgery

- Data from PRONOMOS study published in *The New England Journal of Medicine* and presented during a virtual session of the American College of Cardiology's 69th Annual Scientific Session together with World Congress of Cardiology (ACC.20/WCC Virtual)
- The first study to demonstrate that a Factor Xa inhibitor was superior to enoxaparin in reducing risk of major venous thromboembolism in adult patients who have undergone lower limb nonmajor orthopaedic surgery
- Bleeding rates were low and not significantly different between the Rivaroxaban and enoxaparin groups
- Study is part of an extensive clinical programme exploring Rivaroxaban in people ranging from high risk cancer patients to those having had minor orthopaedic surgery

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Berlin, March 29, 2020 – Bayer's Factor Xa inhibitor, rivaroxaban (Xarelto™) reduced the risk of major venous thromboembolism (VTE) by about 75% in adult patients during a period of immobilization after nonmajor lower limb orthopaedic surgery, when compared to enoxaparin. Bleeding rates were low and not statistically different between both groups.

These data from the clinical phase III trial PRONOMOS were presented as part of a virtual Late-Breaking Clinical Trial Session of the American College of Cardiology's 69th Annual Scientific Session together with World Congress of Cardiology (ACC.20/WCC Virtual) and published simultaneously in *The New England Journal of Medicine*.

"Nonmajor orthopaedic surgery of the lower limbs - like ligament repair of the knee or ankle fracture - can result in a temporary reduction in mobility, placing patients at risk of

developing a VTE. Today, there are limited effective prophylactic treatment options available," said Dr Nadia Rosencher, M.D., Department of Anaesthesia, Intensive Care and Perioperative Medicine at the Université de Paris and investigator of the PRONOMOS study. "This study provides evidence that rivaroxaban has the potential to become an effective preventive option, providing superior protection for these patients compared to the current standard of care."

"Xarelto has already protected millions of patients across the world from VTE," said Dr Joerg Moeller, Member of the Executive Committee of Bayer AG's Pharmaceutical Division and Head of Research and Development. "Bayer has been committed to exploring the benefits of Rivaroxaban in the treatment and prevention of VTE across a broad program of trials including the RECORD program in patients undergoing orthopaedic surgery, the EINSTEIN program in patients with PE and/or DVT including paediatric patients, as well as the CALLISTO program in patients with cancer associated thrombosis."

About PRONOMOS

The international multi-center, randomised double-blind PRONOMOS study included 3,604 adult patients who had undergone nonmajor orthopaedic surgery of the lower limbs and required thromboprophylaxis for at least two weeks. It compared rivaroxaban and enoxaparin in treating this patient population. In the study, 1,809 patients were assigned to receive rivaroxaban 10 mg once daily and 1,795 to receive a subcutaneous injection of 4,000 international units of enoxaparin for the intended treatment duration of 2 to 12 weeks based on medical judgement (according to immobilization).

The primary efficacy outcome of major venous thromboembolism was the composite of symptomatic distal or proximal deep vein thrombosis, pulmonary embolism, or venous thromboembolism-related death during the treatment period; or asymptomatic proximal deep vein thrombosis at the end of treatment. Enoxaparin was used as the comparator in the study as low-molecular-weight heparin is routinely used for thromboprophylaxis after nonmajor orthopaedic surgery in European hospitals. The study was sponsored by the Centre Hospitalier Universitaire de Saint-Étienne, France, and supported by a grant from Bayer.

Efficacy and safety outcomes

For the primary efficacy outcome, rivaroxaban was superior to enoxaparin for the prevention of major VTE. The primary outcome occurred in 4 of 1,661 patients (0.24%) in the rivaroxaban group and in 18 of 1,640 patients (1.10%) in the enoxaparin group (risk ratio 0.25 (95% Confidence Interval (CI) 0.09 - 0.75).

The main safety outcome was the frequency of bleeding events, which was not statistically significantly different between the rivaroxaban and the enoxaparin groups (1.08% and 1.04%, respectively, for major plus nonmajor clinically relevant bleeding (risk ratio 1.04 (95% CI 0.55 - 2.00)). The rates of major bleeding were 0.57% and 0.69%, respectively.

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) 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/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)

Xarelto is approved in more than 130 countries, although the approved labelling, 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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Forward-Looking Statements
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