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News Release

Not intended for U.S. and UK Media

New data for rivaroxaban in patients following the Fontan procedure and at risk for blood clots and blood clot related events

- Pivotal UNIVERSE Phase 3 study published in the *Journal of the American Heart Association* found rivaroxaban (Xarelto™) was associated with numerically fewer thrombotic events and similar safety compared to aspirin in 2-8 years old children with congenital heart disease who have undergone the Fontan procedure
- UNIVERSE data are included in recent New Drug Application to FDA for two new pediatric indications for rivaroxaban

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Berlin, September 27, 2021 – Data from the Phase 3 UNIVERSE study found that treatment with Xarelto™ (rivaroxaban), in an oral suspension formulation, compared to treatment with aspirin, was associated with numerically fewer blood clots and clinical events strongly associated with blood clots in pediatric patients (aged 2-8 years) who have undergone the Fontan procedure.

These findings, which were published this month in the *Journal of the American Heart Association* and were included in a recent New Drug Application to the U.S. Food and Drug Administration for Xarelto, also found that treatment with Xarelto was associated with a similar safety profile compared to aspirin. A comparable and low prevalence of bleeding events in both treatment arms was observed.

“The study results bring us closer to providing pediatricians with a new therapeutic option for these vulnerable and high-risk children,” said Christian Rommel, Member of the Executive Committee of Bayer AG's Pharmaceutical Division and Head of Research and Development. “Xarelto has the most extensive clinical study program of any non-vitamin K antagonist oral anticoagulant and we continue to investigate which patients can benefit most from use of this product.”

Children with congenital heart disease who undergo the Fontan procedure often face significant morbidity and mortality stemming from thrombotic events, especially during the critical 3-to-12-month period following the procedure. Aspirin and older anticoagulants like heparin and vitamin K antagonists (VKAs) have been the most commonly used thromboprophylaxis agents following the Fontan procedure, although lacking health authority approval for this use. However, these antithrombotics have proved problematic in the pediatric setting because of food and drug interactions, parenteral administration, or due to a lack of data from controlled clinical trials recommending optimal dosing or regimen.

“For years, health care providers have had limited options to help reduce the occurrence of potentially fatal thrombotic events that often occur in young children following the Fontan procedure,” said Brian W. McCrindle, M.D., MPH, Pediatric Cardiologist at the Hospital for Sick Children in Toronto. “We now not only have data suggesting that rivaroxaban has a similar positive effect and safety as aspirin, but we also have identified an age-appropriate formulation with precise weight-based dosing to help manage our young patients during a critical time.”

About the UNIVERSE study

A randomized, multicenter, open-label, active controlled, two-part, Phase 3 study, UNIVERSE examined the use of a novel, oral liquid suspension Xarelto formulation in children 2-8 years old with single ventricle physiology who had the Fontan procedure within four months prior to enrollment. From November 2016 to June 2019, a total of 112 participants were enrolled across 35 sites in 10 countries.

The primary safety outcome was major bleeding events according to the International Society on Thrombosis and Haemostasis (ISTH). The secondary safety outcomes were clinically relevant non-major bleeding and trivial (minimal) bleeding events. The primary efficacy outcome was any thrombotic event (venous or arterial) defined as the appearance of a new thrombotic burden within the cardiovascular system noted on either routine surveillance of clinically indicated imaging, or the occurrence of a clinical event known to be strongly associated with thrombus (e.g., stroke or pulmonary embolism). The study was not powered for efficacy outcomes.

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)
• Treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in children and adolescents aged less than 18 years after at least 5 days of initial parenteral anticoagulation treatment

Xarelto is approved in more than 130 countries, although the approved labelling, including the number of indications may differ from country to country. Since launch in 2008, more than 91 million patients have been treated.

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 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 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 2020, the Group employed around 100,000 people and had sales of 41.4 billion euros. R&D expenses before special items amounted to 4.9 billion euros. For more information, go to www.bayer.com.

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Forward-Looking Statements
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