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News Release

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EMA Reaffirms Positive Benefit-Risk Balance of Bayer's Xarelto® for Stroke Prevention in Patients with Atrial Fibrillation

Berlin, February 5, 2016 – The European Medicines Agency (EMA) has reaffirmed the positive benefit-risk balance of Bayer's Xarelto® for stroke prevention in patients with atrial fibrillation. This outcome concludes a CHMP (Committee for Medicinal Products for Human Use) procedure that was initiated to assess whether a potential malfunctioning of the INR device used in the ROCKET AF trial had any impact on the study results. Bayer and its development partner Janssen have undertaken thorough analyses, which were shared with Health Authorities, in particular EMA and the FDA. Separately, the re-analysis conducted by the ROCKET AF Executive Committee, who ran the ROCKET AF trial, was recently published online in the New England Journal of Medicine.

The EMA has concluded that a defect with the INR device used in the ROCKET study does not change its conclusions on the overall safety or benefit-risk balance of Xarelto (rivaroxaban). In particular, the EMA in their announcement states that "after further analyses of the ROCKET study data taking into account the defect in the INR device, EMA's Committee for Medicinal Products for Human Use (CHMP) concluded that any incorrect measurements obtained with the defective device would have had only a marginal effect on the study results, and the safety of Xarelto remains unchanged. In addition, data from other large studies confirmed the comparative safety of the medicine and showed similar rates of bleeding in their warfarin groups." The EMA therefore states: "This means that Xarelto can continue to be used as before, in line with the current prescribing information."

"As a member of the ROCKET AF Executive Committee but equally important as a physician the re-analysis provides me with additional confidence in the strength and robustness of the ROCKET AF trial. It is valuable to be able to provide reassurance to my fellow colleagues but also to our patients and their carers about the evidence for the

benefits of rivaroxaban in protecting people with atrial fibrillation from the risk of a stroke," said Professor Keith A. A. Fox, Duke of Edinburgh Emeritus Professor of Cardiology of the University of Edinburgh, Scotland and Member of the ROCKET AF Executive Committee.

"We are very pleased with EMA's assessment confirming the positive benefit-risk profile of Xarelto for stroke prevention in patients with atrial fibrillation," said Dr. Michael Devoy, Head of Medical Affairs & Pharmacovigilance of Bayer AG's Pharmaceuticals Division and Bayer Chief Medical Officer. "EMA's assessment follows the conclusions from Bayer and Janssen and those from the independent ROCKET AF Executive Committee that the ROCKET AF data are robust. The re-analyses are reassuring and will provide physicians with additional confidence to prescribe Xarelto for their patients with atrial fibrillation at risk of stroke."

In December 2014, Alere Inc. issued a device correction notice for their INR device that is used to monitor INR values in patients using warfarin. Bayer and Janssen were not notified at that time. When the companies became aware of the device correction notice, in September 2015, they promptly reached out to the manufacturer for more information. Upon confirmation from the manufacturer that the devices used in ROCKET AF should have been included in the device correction notice, Bayer and Janssen proactively and quickly notified health authorities around the world, including EMA and the FDA and conducted a number of analyses to assess any potential impact on the primary efficacy and safety results of the ROCKET AF clinical trial. These analyses confirm the results of the ROCKET AF study and the positive benefit-risk profile of Xarelto in patients with non-valvular atrial fibrillation. During the conduct of the ROCKET AF trial (2006-2010), the INR devices were approved for use by the FDA and available on the market in the US and EU (CE mark).

Xarelto is an important anticoagulant used to treat and reduce the risk of life-threatening blood clots. Beyond ROCKET AF, the companies have evaluated the performance of Xarelto in more than 91,000 patients across its approved indications in real-world research following the medicine's approval, and study after study continues to confirm that Xarelto is performing as expected with a positive benefit-risk profile. This is further supported by evidence generated through independent post-marketing studies conducted by regulators and clinicians as well as the study XANTUS which investigated the use of

Xarelto in more than 6,700 patients with AF for stroke prevention in routine clinical practice.

About Xarelto® (Rivaroxaban)
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 seven 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 deep vein thrombosis (DVT) in adults
- The treatment of pulmonary embolism (PE) in adults
- The prevention of recurrent DVT and PE 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 death, myocardial infarction 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

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 therapy 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, please visit https://prescribe.xarelto.com
To learn more about thrombosis, please visit www.thrombosisadviser.com
To learn more about Xarelto, please visit www.xarelto.com

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