Bayer AG
Communications,
Government Relations &
Corporate Brand
51368 Leverkusen
Germany
Tel. +49 214 30-0
www.news.bayer.com

News Release

Not intended for U.S. and UK Media

Bayer comments on article in The British Medical Journal (BMJ) regarding Xarelto®

Berlin, September 29, 2016 – The British Medical Journal (BMJ) has published an article in connection with the anticoagulant Xarelto® on September 28, 2016.

Bayer is concerned about this article and the corresponding press release issued by the BMJ as both include misleading statements which may unnecessarily alarm patients and may result in patients stopping the intake of Xarelto without first consulting their physician, thereby potentially increasing their stroke risk. Bayer would therefore like to stress that if patients have any questions about Xarelto to first consult their doctor.

With regards to the BMJ article, Bayer comments as follows:

Bayer and its partner Janssen Research & Development, LLC have ensured and will continue to ensure that health authorities receive all required and accurate information regarding past and ongoing clinical trials. The companies have properly disclosed safety data to regulators and the safety monitoring board of the ROCKET AF trial and deny the central premise of BMJ's report. Several recent reassessments of the trial data by Bayer and Janssen as well as by the ROCKET AF Executive Committee plus two reviews by the European Medicines Agency (EMA) – including one concluded in July 2016 that assessed the Covance data at the center of BMJ's story – confirm that the benefit-risk profile of Xarelto remains unchanged and favorable. With more than 23 million patients prescribed worldwide, real world research continues to confirm the positive profile of Xarelto.

Importantly, in its press release distributed under embargo on Tuesday, September 27, the BMJ misquoted the conclusion of the EMA. Bayer notified the BMJ of this error and a corrected version of the press release has been published. The correct conclusion by the EMA states ***"that there is sufficient evidence to conclude that the benefit/risk***

balance remains unchanged and favourable for treatment with rivaroxaban in the prevention of thromboembolism in non-valvular atrial fibrillation."

Background on the ROCKET AF Support Program

Early in the conduct of the ROCKET AF trial, a support program was offered to investigators that would provide on demand checks of the point-of-care (POC) device values via a central laboratory (COVANCE). This support program was in addition to the use of an unblinded INR monitor which was described in the protocol for the trial. The aim of this process was two fold: first, to provide clinical assurance to the investigators and second to have a mechanism to return a lab based INR value to the investigator. Importantly, this had to be accomplished while maintaining the integrity of the study blind. Investigators used this option only infrequently. Of the more than 366,000 INR measurements taken during the ROCKET AF clinical trial, investigators submitted 149 samples (0.045%, rivaroxaban 78; warfarin 71) to Covance. These data were not part of the database evaluated to obtain the study results. Bayer and Janssen have provided these data to Health Authorities.

In July 2016, the European Medicines Agency assessed these additional data and came to the conclusion that *"the additional information submitted in relation to the Covance recheck programme do not alter the January 2016 conclusion of LEG 037"* in which the EMA determined that the potential issue with Alere's monitoring device did not impact the conclusions of the ROCKET AF trial. EMA's CHMP July 2016 meeting minutes are available here; EMA's January 2016 conclusion has been published in the February assessment report available here.

About the INR device

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). A device correction notice for the Alere INR device was not issued until December 2014 – four years after the ROCKET AF trial had concluded.

Following review of all information provided, the EMA concluded in their February 2016 assessment report on this topic that Janssen and Bayer were *"not aware of any potential impact of the identified deficiencies of [the] INR device system on the ROCKET studies until Sept[ember] 9, 2015."*

Further evidence on Xarelto

Beyond ROCKET AF, Bayer and its development partner Janssen 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 including the NACORA studies by the French ASNM (French National Agency for Medicines and Health Products Safety), the Dresden Registry, the RELIEF study as well as the REVISIT-US Study. Additionally, the XANTUS study, which investigated the use of Xarelto in more than 6,700 patients with AF for stroke prevention in routine clinical practice as well as a post-marketing safety surveillance (PMSS) study by the U.S. Department of Defense both demonstrated that the rates of major bleeding in patients with atrial fibrillation taking Xarelto for stroke prevention were low in routine clinical practice and consistent with findings from the Phase III ROCKET AF trial. Further, the incidence of major and clinically relevant bleeding seen in warfarin patients in the ROCKET AF trial is comparable to that seen in AF trials involving other non-vitamin K antagonist oral anticoagulants.

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 pulmonary embolism (PE) in adults
- The treatment of deep vein thrombosis (DVT) 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

Bayer: Science For A Better Life
Bayer is a global enterprise with core competencies in the Life Science fields of health care and agriculture. Its products and services are designed to benefit people and improve their quality of life. At the same time, the Group aims to create value through innovation, growth and high earning power. Bayer is committed to the principles of

sustainable development and to its social and ethical responsibilities as a corporate citizen. In fiscal 2015, the Group employed around 117,000 people and had sales of EUR 46.3 billion. Capital expenditures amounted to EUR 2.6 billion, R&D expenses to EUR 4.3 billion. These figures include those for the high-tech polymers business, which was floated on the stock market as an independent company named Covestro on October 6, 2015. For more information, go to www.bayer.com.

Our online press service is just a click away: press.bayer.com
Follow us on Twitter: https://twitter.com/BayerPharma

Contact:
Astrid Kranz, phone +49 30 468-12057
Email: astrid.kranz@bayer.com

Stephanie Prate, phone +49 30 468-196053
Email: stephanie.prate@bayer.com

Find more information at pharma.bayer.com
sp (2016-0232E)

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.