Bayer AG
Investor Relations
51368 Leverkusen
Germany
www.investor.bayer.com

Investor News

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New Late-Breaking Study Data Presented at ACC.17:

Bayer's Rivaroxaban Demonstrated Superior Protection Against Recurrent Venous Thromboembolism Compared with Aspirin in EINSTEIN CHOICE Study

- Study with more than 3,000 patients investigated rivaroxaban 10 mg and 20 mg once daily versus aspirin 100 mg once daily
- Both rivaroxaban treatment arms were superior in preventing recurrent venous thromboembolism while showing comparable and very low rates of major bleeding versus aspirin
- Risk of recurrent thrombosis is up to 10% in the first year if anticoagulation therapy is stopped
- Data were presented in a late-breaking clinical trial session at ACC.17 and published simultaneously in *The New England Journal of Medicine*

Leverkusen, Germany, March 18, 2017 – Bayer AG and its development partner Janssen Pharmaceuticals, Inc. today announced results from the EINSTEIN CHOICE study, which demonstrated that both 10 mg and 20 mg once-daily dosages of its oral Factor Xa inhibitor rivaroxaban (Xarelto®) significantly reduced the risk of recurrent venous thromboembolism (VTE) compared with aspirin 100 mg once daily (acetylsalicylic acid, ASA) in patients who had previously completed 6 to 12 months of anticoagulation therapy for pulmonary embolism (PE) or symptomatic deep vein thrombosis (DVT). Importantly, patients with a definitive need for continued therapeutic anticoagulation beyond the first 6 to 12 months were not included in the study. Rivaroxaban 20 mg once daily (already approved treatment regimen) significantly reduced the risk of recurrent VTE by 66% (relative risk reduction) compared with aspirin 100 mg once daily, whilst rivaroxaban 10 mg once daily significantly reduced the risk of recurrent VTE by 74% (relative risk reduction) compared with aspirin 100 mg once daily. Both rivaroxaban dosages demonstrated comparable and low major bleeding rates (the principal safety

outcome) on the same level as aspirin therapy. Results from EINSTEIN CHOICE were presented today at 8 am EDT as a Late-Breaking Clinical Trial at the American College of Cardiology (ACC) 66th Annual Scientific Session in Washington DC and were simultaneously published in *The New England Journal of Medicine*. Data from EINSTEIN CHOICE have been submitted to the European Medicines Agency (EMA) and will be submitted to other Health Authorities worldwide during the first half of 2017.

Venous thromboembolism, which includes pulmonary embolism and deep vein thrombosis, is the third most common cause of cardiovascular death after heart attack and stroke. In patients with VTE, anticoagulation therapy is recommended for 3 months or longer, depending on the balance between the risk of recurrent VTE and the risk of bleeding.

“In patients with unprovoked VTE or with ongoing risk factors, the risk of recurrence is up to 10% in the first year if anticoagulation therapy is stopped after 3, 6 or 12 months. But many physicians are reluctant to continue anticoagulation therapy for longer durations because they are uncertain of the benefit-risk balance for individual patients,” said Jeffrey Weitz, Professor of Medicine and Biochemistry and Biomedical Sciences, McMaster University, and Executive Director of the Thrombosis and Atherosclerosis Research Institute, Hamilton, Canada and Co-Chair of the EINSTEIN CHOICE Study. “The findings from EINSTEIN CHOICE demonstrated exactly what the study name promised: once approved, rivaroxaban 10 mg once daily will be available to physicians as an additional choice in their armamentarium against recurrent VTE alongside the already approved 20 mg once-daily dose. This flexibility of choices in rivaroxaban doses will then enable physicians to use a precision approach to selecting the most appropriate extended treatment based on assessment of individual patient characteristics.”

“EINSTEIN CHOICE is another example of Bayer’s commitment to help answer important medical questions that arise in daily clinical practice,” said Dr Joerg Moeller, Member of the Executive Committee of Bayer AG's Pharmaceutical Division and Head of Development. “The EINSTEIN Clinical Development Programme, including not only EINSTEIN CHOICE but also EINSTEIN PE, EINSTEIN DVT, and EINSTEIN EXTENSION, has demonstrated the clinical utility of rivaroxaban in the treatment and secondary prevention of venous thromboembolism. These new data from EINSTEIN CHOICE add important additional insights on how best to provide extended protection for patients with a VTE.”

Also presented today during the same Late-Breaking Clinical Trials session at ACC.17 and published simultaneously in *The Lancet* were results from the GEMINI ACS 1 study – a double-blind Phase II study, which randomised 3,037 patients with a recent ACS across 292 sites from 21 countries. The study met its primary endpoint by showing that the combined antithrombotic regimen of rivaroxaban 2.5 mg twice daily in addition to background therapy of clopidogrel or ticagrelor resulted in comparable rates of non-CABG TIMI clinically significant bleeding as aspirin 100 mg once daily in combination with clopidogrel or ticagrelor. Although the rates of the exploratory composite efficacy endpoint were also similar across the treatment groups, GEMINI ACS 1 was not powered to assess the impact on ischemic events.

EINSTEIN CHOICE and GEMINI ACS 1 add to the extensive investigation of rivaroxaban, which, by the time of its completion, is expected to include more than 275,000 patients in both clinical trials and real-world settings.

About EINSTEIN CHOICE

EINSTEIN CHOICE was a randomised, double-blind, superiority study comparing the efficacy and safety of two doses of rivaroxaban (10 mg once daily and 20 mg once daily) with aspirin (100 mg once daily) for the extended treatment of VTE for up to one year in patients with objectively confirmed PE or symptomatic DVT who had previously completed 6 to 12 months of anticoagulation therapy. Aspirin was chosen as the comparator because aspirin 100 mg once daily has previously been shown to reduce the risk of recurrent VTE by approximately 32% without significantly increasing the risk of serious bleeding when compared with placebo, findings which led to its inclusion in current guidelines.

A total of 3,396 patients were randomised from 244 sites in 31 countries. Importantly, patients with a need for continued therapeutic anticoagulation therapy were not included in the study as the objective of the study was to investigate those patients for whom the treating physician was uncertain about the need for continuing anticoagulation therapy at therapeutic doses.

The primary efficacy outcome was fatal or non-fatal symptomatic recurrent VTE (composite of symptomatic recurrent VTE, VTE-related death and unexplained death for which PE could not be excluded). The principal safety outcome was major bleeding. Only the primary efficacy outcome comparison of rivaroxaban 20 mg vs aspirin and rivaroxaban 10 mg vs aspirin was powered for superiority.

EINSTEIN CHOICE demonstrated that rivaroxaban 20 mg once daily significantly reduced the risk of recurrent VTE by 66% (relative risk reduction) compared with aspirin (1.5% vs 4.4%; HR 0.34; 95% CI 0.20-0.59; p<0.001). Rivaroxaban 10 mg once daily significantly reduced the risk of recurrent VTE by 74% (relative risk reduction) compared with aspirin (1.2% vs 4.4%; HR 0.26; 95% CI 0.14-0.47; p<0.001). Rates of major bleeding were comparable and very low across all three treatment arms at rates of 0.5% for rivaroxaban 20 mg once daily, 0.4% for rivaroxaban 10 mg once daily and 0.3% in the aspirin group.

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 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 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 2016, the Group employed around 115,200 people and had sales of EUR 46.8 billion. Capital expenditures amounted to EUR 2.6 billion, R&D expenses to EUR 4.7 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.

Bayer AG, Investor Relations contacts:

Oliver Maier (+49-214-30-81013)
Dr. Jürgen Beunink (+49-214-30-65742)
Peter Dahlhoff (+49-214-30-33022)
Judith Nestmann (+49-214-30-66836)
Constance Spitzer (+49-214-30-33021)
Prof. Dr. Olaf Weber (+49-214-30-33567)

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