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

Investor News

Not intended for U.S. and UK Media

New Study Presented at American Heart Association (AHA) Scientific Sessions 2016:

Bayer's Xarelto® Significantly Reduced Bleeding Compared to VKA in AF-Patients also Receiving Antiplatelet Therapy After Percutaneous Coronary Intervention

- PIONEER AF-PCI is the first randomised study of a non-vitamin K antagonist oral anticoagulant (NOAC) in this patient population
- Data were presented in a late-breaking clinical trial session at AHA and published simultaneously in *The New England Journal of Medicine*

Leverkusen, Germany, November 14, 2016 – Bayer AG today announced results from the Phase IIIb PIONEER AF-PCI study, which demonstrated that two different treatment strategies with its oral Factor Xa inhibitor Xarelto® (rivaroxaban) both significantly reduced the risk of bleeding compared to a vitamin K antagonist (VKA) treatment strategy in patients with non-valvular atrial fibrillation (AF) after percutaneous coronary intervention (PCI) with stent placement. Specifically, rivaroxaban 15 mg once daily in combination with single antiplatelet therapy significantly reduced the rate of clinically significant bleeding by 41 per cent (relative risk reduction; equivalent to 9.9 per cent absolute risk reduction) compared to VKA plus dual antiplatelet therapy (DAPT) through 12 months of randomised therapy in these patients. Rivaroxaban 2.5 mg twice daily in combination with DAPT reduced the rate of clinically significant bleeding compared to VKA + DAPT by 37 per cent (relative risk reduction; equivalent to 8.7 per cent absolute risk reduction) through 12 months of randomised therapy, which was also statistically significant. Similar rates for the exploratory efficacy endpoint (cardiovascular death, MI, stroke, and stent thrombosis) were observed; however, the study was not powered for statistical significance on efficacy. Results from PIONEER AF-PCI – the first randomised trial of a non-vitamin K antagonist oral anticoagulant (NOAC) in this patient population – were presented today as a Late-Breaking Clinical Trial at American Heart Association (AHA) Scientific Sessions 2016 in New Orleans, LA, USA and published simultaneously in *The New England*

Journal of Medicine. Furthermore, a supporting sub-analysis of PIONEER AF-PCI showing significantly fewer rates of all-cause mortality or recurrent hospitalisation due to adverse events for patients taking rivaroxaban plus antiplatelet therapy compared to those on VKA plus antiplatelet therapy was also simultaneously published in *Circulation*.

“Patients with non-valvular AF who undergo PCI are at increased risk of blood clots, which can trigger severe consequences including stroke, myocardial infarction and stent thrombosis. In order to reduce the risk of these, patients are currently being treated with a combination therapy that increases their risk of bleeding,” said C. Michael Gibson, M.S., M.D., Professor of Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center in Boston, USA and the Principal Investigator of the PIONEER AF-PCI study. “Now, the PIONEER AF-PCI study demonstrated that statistically one bleeding event could be prevented if 11 patients were treated with the 15 mg once-daily rivaroxaban treatment strategy, thus offering physicians essential guidance to make more informed treatment decisions for this patient population in the future.”

“PIONEER AF-PCI answers an important medical question because it is potentially relevant for the 20-45% of AF patients that also have coronary artery disease and are at risk of having to have a PCI. The actual rate of PCI procedures in AF patients is approximately 1% per year,” said Dr Michael Devoy, Head of Medical Affairs & Pharmacovigilance of Bayer AG’s Pharmaceuticals Division and Bayer Chief Medical Officer.

Despite this, there was a lack of clinical evidence to guide best possible treatment strategies in these patients. Current Guidelines and consensus / position papers recommend a combination of antiplatelet and anticoagulant therapies for the initial phase after PCI in patients with AF – a treatment approach that has been associated with an increased risk of bleeding, including intracranial bleeding.

PIONEER AF-PCI adds 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 PIONEER AF-PCI

PIONEER AF-PCI was an open-label, randomised Phase IIIb study, designed to determine the safety of two rivaroxaban treatment regimens versus a dose-adjusted vitamin K antagonist (VKA) treatment strategy after percutaneous coronary intervention (PCI) with stent placement in patients with non-valvular atrial fibrillation (AF). PIONEER AF-PCI included 2,124 patients worldwide in 26 different countries.

The primary endpoint of the study was the occurrence of clinically significant bleeding, defined as a composite of TIMI major bleeding, TIMI minor bleeding and bleeding requiring medical attention through 12 months of randomised therapy. All patients were randomised in a 1:1:1 ratio into three treatment arms:

- Arm 1: Rivaroxaban 15 mg once daily (or 10 mg od for patients with moderate renal impairment [CrCl: 30 – 50 ml/min]) plus clopidogrel (or prasugrel or ticagrelor) for 12 months
- Arm 2: Rivaroxaban 2.5 mg twice daily plus a pre-specified duration of 1, 6 or 12 months (investigator determined) of DAPT consisting of low-dose acetylsalicylic acid (ASA) + clopidogrel (or prasugrel or ticagrelor), followed by rivaroxaban 15 mg once daily (or 10 mg od for patients with moderate renal impairment) in combination with low-dose ASA to end of month 12
- Arm 3: Triple therapy consisting of dose-adjusted VKA (target INR of 2.0–3.0) plus DAPT (as in arm 2) for a pre-specified duration of 1, 6 or 12 months (investigator determined), followed by dose-adjusted VKA (target INR of 2.0–3.0) in combination with low-dose ASA to end of month 12

PIONEER AF-PCI demonstrated that rivaroxaban 15 mg once-daily plus clopidogrel significantly reduced the rate of clinically significant bleeding by 41 per cent (relative risk reduction) compared with triple therapy consisting of a VKA in combination with dual antiplatelet therapy (DAPT) (16.8% vs 26.7%; HR 0.59; 95% CI 0.47-0.76; p<0.001) through 12 months of randomised therapy. Rivaroxaban 2.5 mg twice-daily in combination with DAPT reduced the rate of clinically significant bleeding compared to VKA + DAPT by 37 per cent (relative risk reduction) through 12 months of randomised therapy, which was also statistically significant (18.0% vs 26.7%; HR 0.63; 95% CI 0.50-0.80; p<0.001). Similar rates for the exploratory efficacy endpoint (cardiovascular death, MI, stroke, and stent thrombosis) were observed; however, the study was not powered for statistical significance on efficacy.

Additionally, a separate sub-analysis of PIONEER AF-PCI, published simultaneously in *Circulation*, showed that both rivaroxaban treatment regimens resulted in significantly fewer rates of all-cause mortality or recurrent hospitalisation due to adverse events (bleeding, a cardiovascular cause or other cause) than the VKA treatment strategy. The risk of all-cause mortality or recurrent hospitalisation was 34.9 per cent in the rivaroxaban 15 mg once-daily group (p=0.008) and 31.9 per cent in the rivaroxaban 2.5 mg twice-daily group (p=0.002) compared to 41.9 per cent in the VKA group. When looking specifically at re-hospitalisation, both rivaroxaban treatment groups had significantly lower rates of all-cause re-hospitalisation, with 34.1 per cent in the rivaroxaban 15 mg once-daily group (p=0.005) and 31.2 per cent in the rivaroxaban 2.5 mg twice-daily group (p=0.001) compared to 41.5 per cent in the VKA 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 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.

Bayer AG, Investor Relations contacts:

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)

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.