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Investor News

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Bayer's rivaroxaban submitted to U.S. FDA for approval in patients with coronary and/or peripheral artery disease

- The rivaroxaban vascular dose, 2.5 mg twice daily plus aspirin 100 mg once daily, demonstrated a 24% reduction in the combined risk of stroke, cardiovascular death and heart attack
- The application for marketing approval is based on the COMPASS study

Leverkusen, December 11, 2017 – Bayer´s development partner, Janssen Research & Development, LLC has submitted a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for the rivaroxaban (Xarelto®) vascular dose, 2.5 mg twice daily, to be used in combination with low dose aspirin. The application requests approval of two new indications for the rivaroxaban vascular dose: for reducing the risk of major cardiovascular (CV) events such as CV death, heart attack or stroke in patients with chronic coronary and/or peripheral artery disease (CAD/PAD), and for reducing the risk of acute limb ischemia in patients with PAD. This application is based on the Phase III COMPASS study.

"This submission represents an important step forward in addressing the often devastating effects of coronary and peripheral artery disease," said Dr Joerg Moeller, Member of the Executive Committee of Bayer AG's Pharmaceutical Division and Head of Development. "If approved, the combination of the rivaroxaban vascular dose plus aspirin will provide an effective treatment option for the millions of patients living with CAD and PAD."

It is estimated that cardiovascular disease, which includes CAD and PAD, is responsible for some 17.7 million deaths every year, representing 31% of all global deaths[1]. Additionally, patients with cardiovascular disease have a reduction in life expectancy of over 7 years[2]. CAD and PAD are caused by atherosclerosis, a chronic, progressive disease which is characterized by a build-up of plaque in the arteries[3,4]. Patients with

these conditions are at risk of thrombotic events which may lead to disability, loss of limb and loss of life[4,5,6]. Current treatment guidelines recommend antiplatelet therapies such as aspirin alone, although this has been shown to be only modestly effective[7].

About COMPASS

As well as demonstrating a significant reduction in the combined efficacy endpoint of major adverse cardiovascular events (MACE), the COMPASS study also showed that the rivaroxaban vascular dose, 2.5 mg twice daily, plus aspirin 100 mg once daily, resulted in a significant reduction in stroke (42%) and CV death (22%) compared to aspirin 100 mg once daily alone. Furthermore, the combination regimen was associated with a 20% improvement in net clinical benefit, defined as the reduction in stroke, CV death, and heart attack balanced against irreversible harm, defined as a composite of all fatal or irreversible safety events.

Bleeding incidence rates were low, and while there was an increase in major bleeding, notably there was no significant increase in fatal or intracranial bleeding. Importantly, in the PAD patient population, the combination of major adverse limb events (MALE) plus all major amputations of a vascular cause were reduced significantly. The results of the COMPASS study were presented at the European Society of Cardiology (ESC) Congress 2017 and published simultaneously in *The New England Journal of Medicine* in August 2017. Additional findings and analysis from the COMPASS study have also been published in two publications in *The Lancet* in November 2017[8,9].

COMPASS is part of the extensive evaluation of rivaroxaban, which, by the time of completion, will include more than 275,000 patients in clinical trials and real-world studies. In addition to COMPASS, Bayer is investigating rivaroxaban in other studies in the area of cardiovascular disease and vascular protection including VOYAGER PAD (patients with PAD undergoing peripheral artery interventions) and COMMANDER-HF (patients with chronic heart failure and significant CAD).

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 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) and 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 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
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 99,600 people and had sales of EUR 34.9 billion. Capital expenditures amounted to EUR 2.2 billion, R&D expenses to EUR 4.4 billion. For more information, go to www.bayer.com.

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