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Investor News

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Bayer Extends Clinical Investigation of Rivaroxaban into Important Areas of Unmet Medical Need in Arterial Thromboembolism

New studies expand investigation of rivaroxaban to more than 275,000 patients

Leverkusen, Germany, August 29, 2014 – Bayer HealthCare and its development partner Janssen Research & Development, LLC announced today an expansion of the global clinical development programme for the oral Factor Xa inhibitor rivaroxaban for the prevention of potentially deadly blood clots in patients at risk of arterial thromboembolism. Three new studies will investigate the efficacy and safety of rivaroxaban in:

- Patients who have suffered an embolic stroke of undetermined source (ESUS)
- Patients with peripheral artery disease (PAD) undergoing peripheral artery interventions
- Patients who have had an acute coronary syndrome (ACS)

“Together with our partner Janssen, we are committed to further investigate the potential benefits of rivaroxaban in areas of significant unmet medical need,” said Dr Joerg Moeller, Member of the Bayer HealthCare Executive Committee and Head of Global Development. “Rivaroxaban is already approved to prevent and treat more venous and arterial thromboembolic conditions than any other novel oral anticoagulant. However, areas of unmet medical need still exist where rivaroxaban could potentially benefit even more patients at risk of the serious and often life-threatening diseases caused by blood clots.”

Rivaroxaban (Xarelto®) has already been approved for five indications in seven distinct areas of use. Yet the global burden of thrombosis-related diseases remains significant in a number of areas of unmet medical need. While the ongoing programme for rivaroxaban, including Phase III studies like COMPASS, COMMANDER-HF, MARINER, and

EINSTEIN CHOICE, addresses some of these, the medical need in three additional areas is still high:

- **Embolic stroke of undetermined source (ESUS)**
  NAVIGATE ESUS is a global Phase III indication-seeking study, designed to evaluate rivaroxaban in patients with embolic stroke of undetermined source. The study will include approximately 7,000 patients and be conducted in more than 25 countries.

  ESUS accounts for approximately 25 per cent of ischaemic strokes, but there is limited knowledge or data available to guide treatment decisions regarding the secondary prevention of stroke in these patients. “The ROCKET AF study showed that once-daily rivaroxaban was effective and well-tolerated among patients who have atrial fibrillation with and without previous stroke or transient ischaemic attack,” said Dr Robert G. Hart, M.D., Professor of Medicine (Neurology), McMaster University, Hamilton, Ontario, Canada. “Based on the findings from ROCKET AF, we will investigate the potential clinical value of once-daily rivaroxaban in preventing recurrence of stroke in patients with embolic stroke of undetermined source – an important unmet need in stroke prevention.”

- **Peripheral artery disease (PAD)**
  VOYAGER PAD will explore the potential benefits of rivaroxaban in reducing thrombotic vascular complications in patients with peripheral artery disease undergoing peripheral artery interventions. This global Phase III indication-seeking study will enroll more than 5,000 patients across more than 20 countries.

  PAD affects approximately 202 million people worldwide, and the progressive build-up of plaque inside the arteries can slowly reduce the blood flow to the limbs and the heart. Patients with PAD are not only at an increased risk of atherothrombotic events such as stroke, heart attack, or cardiovascular death, but also of amputations and acute limb ischaemia. “Building on the results of the ATLAS ACS 2-TIMI 51 study in acute coronary artery disease, this study will investigate whether rivaroxaban can provide similar protection to patients with symptomatic PAD undergoing peripheral revascularisation procedures,” said Prof William R. Hiatt, M.D., Professor of Medicine / Cardiology, University of Colorado School of Medicine, President CPC Clinical Research, Denver, USA.

- **Acute Coronary Syndrome (ACS)**
  GEMINI ACS 1 is a global Phase II study, designed to evaluate rivaroxaban for long-term prevention in patients who have suffered an acute coronary syndrome (ACS). The study will include 2,000 – 3,000 patients in more than 10 countries. If successful, GEMINI ACS 1 will be followed by a confirmatory, fully powered, global Phase III study.

  The ATLAS ACS 2-TIMI 51 trial demonstrated that the Dual Pathway Strategy of rivaroxaban 2.5 mg twice daily in combination with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine resulted in significant reductions in cardiovascular death, heart attack, stroke and stent thrombosis in selected high-risk patients who had an acute coronary syndrome (ACS) event with elevated cardiac biomarkers. “As a next step we will investigate the benefits of the Dual Pathway Strategy of rivaroxaban in combination with single antiplatelet treatment, including the novel antiplatelet agents, for long-term secondary prevention after ACS in a broader range of patients,” said Prof E. Magnus Ohman, M.D., Professor of Medicine, Duke Clinical Research Institute, Durham, North Carolina, USA.

The extensive evaluation of rivaroxaban to protect different patient populations at risk of venous and arterial thromboembolism (VAT), makes it the most studied novel OAC in the world. The investigation of rivaroxaban will include more than 275,000 patients in both clinical trials and real world settings.

About Xarelto® (Rivaroxaban)
Rivaroxaban is the most broadly indicated novel oral anticoagulant and is marketed under the brand name Xarelto®. Xarelto is approved for five indications across seven distinct areas of use:

- 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 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 125 countries.

Rivaroxaban was discovered by Bayer HealthCare, and is being jointly developed with Janssen Research & Development, LLC. Xarelto is marketed outside the U.S. by Bayer HealthCare and in the U.S. by Janssen Pharmaceuticals, Inc. (a Johnson & Johnson Company).

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

About Bayer HealthCare
The Bayer Group is a global enterprise with core competencies in the fields of health care, agriculture and high-tech materials. Bayer HealthCare, a subgroup of Bayer AG with annual sales of EUR 18.9 billion (2013), is one of the world’s leading, innovative companies in the healthcare and medical products industry and is based in Leverkusen,

Germany. The company combines the global activities of the Animal Health, Consumer Care, Medical Care and Pharmaceuticals divisions. Bayer HealthCare's aim is to discover, develop, manufacture and market products that will improve human and animal health worldwide. Bayer HealthCare has a global workforce of 56,000 employees (Dec 31, 2013) and is represented in more than 100 countries. More information is available at www.healthcare.bayer.com

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