Bayer HealthCare

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Bayer Pharma AG
13342 Berlin
Germany
Tel. +49 30 468-1111
www.bayerpharma.com

News Release

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Treatment and prevention of venous blood clots:

Results from Phase III Pooled EINSTEIN Studies Reaffirm Bayer's Xarelto® as an Effective Single-Drug Solution for Venous Thromboembolism

- Blood clots obstructing blood flow in deep veins or in the lungs kill one person every 37 seconds in the Western World
- Pooled data of over 8,000 patients reaffirm the improved benefit-risk profile of Xarelto as an effective single-drug solution compared with the traditional dual-drug therapy
- Xarelto associated with 46% less major bleeding events, including fatal bleeding compared to standard dual-drug therapy, whilst having similar overall incidence rates for the principal safety outcome of major or non-major clinically relevant bleeding
- Additionally, a sub-analysis of the EINSTEIN DVT study published in the journal *Thrombosis and Haemostasis* confirms that Xarelto improves treatment satisfaction compared with traditional dual-drug therapy and indicates better adherence and persistence in long-term prevention of recurrent venous blood clots compared with vitamin K antagonists (VKAs)
- Bayer's 'Responsible Use Programme' for physicians and patients supports best practice, helping to achieve improved clinical outcomes with 'Xarelto'

Berlin, Germany, September 20, 2013 – Data from the Phase III EINSTEIN clinical trial programme published today in the *Thrombosis Journal* underline that single-drug therapy with Bayer HealthCare's novel oral anticoagulant Xarelto® (rivaroxaban) is effective in both the treatment and subsequent prevention of recurrent deep vein thrombosis (DVT) and pulmonary embolism (PE), with an overall comparable safety to the traditional dual-drug therapy.

In addition, compared to the traditional dual-drug approach of injectable low molecular weight heparin (LMWH) followed by a vitamin K antagonist (VKA), Xarelto significantly reduced the rate of major bleeding events by 46 per cent, including the risk of fatal bleeding, whilst offering an improved benefit-risk profile regardless of patient age, frailty, gender, weight or renal function.

“Today’s publication of these impressive data further highlights the potential of this drug to change current clinical practice in both the treatment of initial acute DVT and PE, as well as the prevention of recurrent DVT and PE,” said Dr Alexander T. Cohen, King’s College Hospital, London, and member of the Steering Committee of the EINSTEIN studies. “The unique single-drug therapy of rivaroxaban has the potential to not only improve clinical outcomes, but also reduce the overall burden of anticoagulation therapy by providing continuous patient management from hospital to home while avoiding the need for injections or routine coagulation monitoring.”

Additionally, a sub-analysis of the EINSTEIN DVT study recently pre-published online in the journal *Thrombosis and Haemostasis* confirms that Xarelto improves treatment satisfaction compared with traditional dual-drug therapy. The data also indicate improved adherence and persistence with Xarelto in long-term prevention of recurrent venous blood clots compared with VKAs such as warfarin. These findings complement an analysis of patient-reported satisfaction in the EINSTEIN PE study, and indicate an important adherence and persistence benefit with Xarelto in both acute treatment and long-term prevention regardless of the type of venous blood clot experienced.

“These analyses add to the large amount of clinical data and real-life experience supporting Xarelto in the management of both venous and arterial blood clots, providing further reassurance regarding the clinical use of Xarelto across a broad range of clinical settings,” said Dr. Kemal Malik, Member of the Bayer HealthCare Executive Committee and Head of Global Development.

Xarelto is approved for five indications across seven distinct areas of use, consistently protecting patients across more venous and arterial thromboembolic (VAT) conditions than any other novel oral anticoagulant.

About The EINSTEIN Clinical Trial Programme and Pooled Analysis
The pivotal EINSTEIN Clinical Trial Programme comprises three Phase III studies evaluating rivaroxaban alone versus the dual-drug regimen of low molecular weight heparin (LMWH) and a vitamin K antagonist (VKA) in the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and the prevention of recurrent DVT and PE.

In the pooled analysis of over 8,000 patients, rivaroxaban showed non-inferiority versus the LMWH enoxaparin and VKA in terms of efficacy (HR 0.89 (95% CI 0.66-1.19), p=<0.0001) and similar overall incidence rates to enoxaparin and VKA for the principal safety outcome of major or non-major clinically relevant bleeding (HR 0.93 (95% CI 0.81-1.06), p=0.272). Importantly, rivaroxaban showed a significant reduction in major bleeding (HR 0.54 (95% CI 0.37-0.79), p=0.002) over traditional dual-drug therapy. Overall, the principal safety results were consistent regardless of the patient's age, frailty, weight, gender and renal function. Results from the pooled analysis were previously presented at the 54th American Society of Hematology (ASH) Annual Meeting in Atlanta in December 2012.

Xarelto is approved as the single-drug solution for the treatment of DVT and PE as well as for the prevention of recurrent DVT and PE in adults in a number of countries worldwide including Europe and the U.S.

About Venous Arterial Thromboembolism (VAT)
Thrombosis is the formation of a blood clot inside a blood vessel, blocking a vein (venous thrombosis) or artery (arterial thrombosis). Venous Arterial Thromboembolism (VAT) is caused when some or all of a clot detaches and is moved within the blood stream until it obstructs a smaller vessel. This can result in damage to vital organs, because the tissue beyond the blockage no longer receives nutrients and oxygen.

VAT is responsible for a number of serious and life threatening conditions:

- Venous Thromboembolism (VTE) occurs when part of a clot formed in a deep vein, for example in the leg (known as deep vein thrombosis, or DVT), is carried to the lung, via the heart, preventing the uptake of oxygen. This is known as a pulmonary embolism (PE), an event which can be rapidly fatal. Blood clots that obstruct blood

flow in deep veins or in the lungs kill one person every 37 seconds in the Western World

- Arterial Thromboembolism occurs when oxygenated blood flow from the heart to another part of the body (via an artery) is interrupted by a blood clot. If this occurs in a vessel supplying blood to the brain, it can lead to a stroke, an event that can be severely debilitating or fatal. If it occurs in a coronary artery, it can lead to acute coronary syndrome (ACS), a complication of coronary heart disease which includes conditions such as myocardial infarction and unstable angina

VAT is responsible for significant morbidity and mortality, and requires active or preventative treatment to avoid potentially serious or fatal patient outcomes.

To learn more about VAT, please visit www.VATspace.com

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, consistently protecting patients across more venous and arterial thromboembolic (VAT) conditions than any other novel OAC:

- 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 venous thromboembolism (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 a thienopyridine (clopidogrel or ticlopidine)

Whilst licences may differ from country to country, across all indications Xarelto is approved in more than 120 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 18.6 billion (2012), 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 55,300 employees (Dec

31, 2012) and is represented in more than 100 countries. More information at www.healthcare.bayer.com.

Our online press service is just a click away: press.healthcare.bayer.com

Contact:
Astrid Kranz, Tel. +49 30 468-12057
E-Mail: astrid.kranz@bayer.com

Stephanie Prate, Tel +49 30 468-196053
E-Mail: stephanie.prate@bayer.com

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