



News Release

Venous Blood Clot Prevention after Hip Replacement Surgery:

***The Lancet* Publishes Results from the Landmark Phase III Rivaroxaban Study RECORD2**

- Trial involving over 2.500 patients after hip replacement surgery
- Five weeks of Rivaroxaban compared to two weeks enoxaparin
- Extended Rivaroxaban treatment regimen significantly more effective with comparable low bleeding rates

Berlin, June 25, 2008 — Data published online today in *The Lancet* demonstrate that extended duration treatment with the investigational anticoagulant, rivaroxaban (Xarelto[®]), taken as one tablet daily, substantially reduced the number of venous blood clots in patients undergoing total hip replacement surgery compared with short duration enoxaparin followed by placebo. The 5-week rivaroxaban regimen, despite being a longer course of treatment, showed a similar low rate of bleeding when compared to the 2-week enoxaparin regimen. This further demonstrates the strong safety profile of rivaroxaban when compared to enoxaparin followed by placebo. Rivaroxaban is being jointly developed by Bayer HealthCare AG and Johnson & Johnson Pharmaceutical Research & Development, L.L.C..

The *Lancet* has also published an accompanying commentary by Dr. John W Eikelboom and Dr. Jeffrey I Weitz entitled, "Selective factor Xa inhibition for thromboprophylaxis", which provides an additional independent perspective on the findings.

The RECORD2 (**RE**gulation of **Co**agulation in major **O**rthopedic surgery reducing the **R**isk of **D**VT and **PE**) data show that 5 weeks of treatment with rivaroxaban (10mg tablet once-daily) a direct Factor Xa inhibitor, provided patients undergoing total hip replacement surgery with a statistically significant 79% relative risk reduction (RRR) in total venous thromboembolic events ($p < 0.0001$) compared to 2 weeks of subcutaneous enoxaparin

(40mg injection once-daily) followed by placebo. Major bleeding rates were identical and very low in both treatment groups (< 0.1% in both groups). Top-line results from RECORD2 were previously presented at the annual meeting of the American Society of Hematology in December 2007.

“This study is the largest to date evaluating the need for and benefits of continuing measures beyond hospital stay to prevent blood clots after major orthopaedic surgery. It showed that continued use of the new orally active anticoagulant drug rivaroxaban for up to 5 weeks after hip replacement surgery substantially reduced the risk of serious blood clots relative to the comparator treatment of two weeks enoxaparin followed by placebo and provides convincing evidence for the need for extended treatment”, said Prof. Ajay K Kakkar, Principal Investigator of the RECORD2 study, and Professor for Surgical Sciences at Barts and the London School of Medicine and Dentistry; and Director of the Thrombosis Research Institute, London, UK.

RECORD2 is the largest Phase III, prospective, randomized, double-blind trial to date to evaluate short versus extended thromboprophylaxis in high-risk surgical patients. It is part of the global RECORD program of clinical studies, comprising four pivotal Phase III trials of 12,729 patients. Together, the results of these four studies have consistently demonstrated the high clinical efficacy of rivaroxaban in preventing venous blood clots following major orthopaedic surgery without compromise in terms of safety, in particular bleeding.

“RECORD2 study results provide further indication of the substantial benefit rivaroxaban can bring to patients undergoing total hip replacement surgery without increasing their risk of serious bleeding complications or other adverse events that may affect surgical outcomes,” commented Frank Misselwitz, M.D., PhD, Head of Cardiovascular Clinical Development, Bayer HealthCare AG.

Blood clots are a potentially deadly but preventable complication of major orthopedic surgery such as elective total hip or knee replacement surgery. Patients have a high risk of developing a blood clot for at least two months after surgery. Current treatments for VTE prevention have drawbacks in the outpatient setting, such as the need for regular injections or routine blood monitoring. Consequently, there is a high medical need for new anticoagulants that overcome these limitations.

RECORD2 Study Details

RECORD2 compared the safety and efficacy of an extended rivaroxaban treatment to short duration treatment with enoxaparin in 2,509 patients undergoing total hip replacement surgery. Patients were randomized to receive rivaroxaban (10mg tablet once-daily) for 35+/-4 days or subcutaneous enoxaparin (40mg injection once-daily) for 10–14 days, followed by placebo.

Overall, RECORD2 demonstrated a 79% RRR in total VTE (the primary efficacy endpoint which encompasses the composite of deep vein thrombosis, non-fatal pulmonary embolism and all-cause mortality) for the extended rivaroxaban treatment when compared with the short duration treatment with enoxaparin ($p<0.0001$), and an 88% RRR ($p<0.0001$) in major VTE (the main secondary efficacy endpoint which focuses on proximal DVT and VTE-related events).

The primary safety endpoint was major bleeding. The superior efficacy of rivaroxaban was not associated with any significant differences in the incidence of major bleeding between rivaroxaban and enoxaparin groups (<0.1% in both groups). Rivaroxaban has not been associated with compromised liver function.

Notes to editors:

Unmet Needs in Venous Thromboembolism (VTE)

In the EU, blood clots exceed 1.5 million events annually and are responsible for killing 544,000 people each year – more than breast cancer, prostate cancer, HIV/AIDS and road traffic accidents combined.

VTE is a serious life-threatening condition. It includes deep vein thrombosis (DVT) – a blood clot in a deep vein (usually in the leg) – and pulmonary embolism (PE) – a blood clot in the lungs. These clots often break apart and travel through the bloodstream, blocking blood flow to vital organs. During hip or knee replacement procedures, the large veins of the leg that carry blood back to the heart are damaged which significantly increases the VTE risk for patients undergoing such major orthopedic surgery. In fact, venous blood clots occur in 40-60% of patients undergoing major orthopedic surgery and not receiving preventative care.

An estimated 815,000 hip replacement procedures were performed in the US and Europe in 2005 while the number of knee replacement procedures was estimated to be 761,000 and is expected to significantly increase in the next years. But the threat stretches beyond orthopedic surgeries: Blood clots are one of the leading causes of global disease and death in many patient populations, including those with atrial fibrillation at risk for stroke, those at risk for acute myocardial infarction (heart attack) and acutely ill hospitalized patients, such as those with cancer.

To learn more about VTE please visit www.thrombosisadviser.com

About the RECORD program

RECORD (**RE**gulation of **CO**agulation in major **OR**thopedic surgery reducing the **R**isk of **DVT** and **PE**), is a global program of clinical trials involving 12,729 patients, comparing rivaroxaban with enoxaparin in patients following either total knee or hip replacement surgery.

- In **RECORD1**, rivaroxaban demonstrated a 70% relative risk reduction (RRR) in total VTE in patients undergoing total hip replacement (THR) surgery compared with enoxaparin, with a similar safety profile. The duration of thromboprophylaxis in both treatments was five weeks. Top-line results from the study were first presented at the annual meeting of the American Society of Hematology (ASH) in December 2007.
- In **RECORD2**, extended-duration rivaroxaban (35+/-4 days) demonstrated a 79% RRR in total VTE and a similar rate of major bleeding in patients undergoing THR surgery compared to patients dosed with short-duration therapy with enoxaparin (10–14 days) followed by placebo.
- In **RECORD3**, rivaroxaban demonstrated 49% RRR in total VTE in patients undergoing total knee replacement (TKR) surgery compared to enoxaparin, with a similar safety profile. Both treatments were dosed for 10–14 days. Top-line results from this study were first presented at the International Society on Thrombosis and Haemostasis (ISTH) Congress in July 2007.
- In **RECORD4**, 10mg once-daily rivaroxaban was compared to the U.S.-approved regimen for enoxaparin of 30mg injected twice-daily. Rivaroxaban demonstrated a 31% RRR in total VTE in patients undergoing TKR surgery compared to enoxaparin, with a similar safety profile. Both treatments were continued for 10–14 days. Top-line results from this study were first presented in May 2008 at the

annual meeting of the European Federation of National Associations of Orthopaedics & Traumatology (EFORT).

About Rivaroxaban

The extensive clinical trial program for rivaroxaban makes it the most studied, oral, direct Factor Xa inhibitor in the world today. Based on the clinical evidence in more than 20,000 patients, rivaroxaban has not been associated with compromised liver function. A more definitive statement will be made once the data from long-term exposure to rivaroxaban in the VTE treatment and stroke prevention in atrial fibrillation (SPAF) programs are available. Almost 50,000 patients are expected to be evaluated in the already finalized and ongoing total clinical development program.

Bayer HealthCare submitted a regulatory filing to the European Agency for the Evaluation of Medicinal Products (EMA) at the end of October 2007 for approval to market rivaroxaban in the EU for the prevention of VTE in patients undergoing major orthopaedic surgery of the lower limbs. To date, the drug has been filed in more than 10 countries, including Canada and China, and is also expected to be filed for approval in the U.S. in mid 2008, where if approved, it will be commercialized by Scios Inc. and Ortho-McNeil, Inc., both of which are wholly-owned subsidiaries of Johnson & Johnson.

The trade name of rivaroxaban is expected to be Xarelto[®], pending health authority approval.

About Bayer HealthCare

The Bayer Group is a global enterprise with core competencies in the fields of health care, nutrition and high-tech materials. Bayer HealthCare, a subsidiary of Bayer AG, 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, Diabetes Care and Pharmaceuticals divisions. The pharmaceuticals business operates under the name Bayer Schering Pharma. Bayer HealthCare's aim is to discover and manufacture products that will improve human and animal health worldwide. Find more information at www.bayerhealthcare.com.

Bayer Schering Pharma is a worldwide leading specialty pharmaceutical company. Its research and business activities are focused on the following areas: Diagnostic Imaging,

General Medicine, Specialty Medicine and Women's Healthcare. With innovative products, Bayer Schering Pharma aims for leading positions in specialized markets worldwide. Using new ideas, Bayer Schering Pharma aims to make a contribution to medical progress and strives to improve the quality of life. Find more information at www.bayerscheringpharma.de.

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Forward-Looking Statements

This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer Group or subgroup 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.