



## Fact Sheet

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Bayer Schering Pharma Development Projects

Business Unit: Hematology/Cardiology

### **Rivaroxaban: A novel oral, once-daily anticoagulant in advanced development for the prevention and treatment of thromboembolic diseases**

Potential attributes:

- Few interactions with other drugs or foods
  - No need for routine blood coagulation monitoring
  - Wide therapeutic window
  - Use in both acute and chronic indications
  - Use in hospital and home settings
  - Fixed doses with no need for dose adjustment for age, gender, or weight
  - Oral administration
  - A strong safety and efficacy profile
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Status: June 2007

<b>Project description</b>	<b>At a glance</b>
<p>Rivaroxaban is a novel oral, once-daily anticoagulant (a drug that has the potential to prevent or treat blood clots) in advanced clinical development for the prevention and treatment of thromboembolic disease in both acute and chronic segments, enabling administration in both the hospital and home settings. Rivaroxaban specifically inhibits Factor Xa in the coagulation system, thereby controlling the generation of thrombin (an enzyme that facilitates clotting).</p>	<p><b>Name of active substance</b> Rivaroxaban (BAY 59-7939)</p>

<p><b>Clinical development</b></p> <p>Rivaroxaban is in advanced clinical development for the effective prevention and treatment of venous and arterial thrombosis in acute and chronic indications. The development program is comprehensive, with almost 40,000 patients expected to be evaluated in 13 Phase II-III studies, spanning several indications, including prevention of venous thromboembolism (VTE) in patients undergoing major orthopedic surgery, treatment of VTE, prevention of stroke in patients with atrial fibrillation, and prevention of major cardiovascular events in patients with acute coronary syndrome.</p> <p>Results from four Phase II studies in the prevention of VTE after major orthopedic surgery have shown that rivaroxaban has an efficacy and safety profile similar to that of the current therapeutic standard. In contrast to the subcutaneously injected standard therapy, low molecular weight heparins (LMWHs), rivaroxaban is expected to be administered once daily in tablet form. Rivaroxaban is currently undergoing extensive testing in Phase III clinical trials.</p> <p><b>Medical background</b></p> <p>Patients are at an increased risk for thromboembolic disease following orthopedic surgery. Currently, patients undergoing orthopedic surgery are given LMWHs or vitamin K antagonists (VKAs) to prevent VTE. Parenteral administration of LMWHs limits their use outside the hospital setting, making it difficult to follow therapy guidelines – which recommend treatment for up to several weeks. To date, vitamin K antagonists are the only treatment that can be administered orally, but their onset of action is slow and their effectiveness varies significantly from one patient to another. Moreover, these substances have numerous interactions with other drugs and with some foods, which means their efficacy needs to be monitored closely by regular blood tests and the dosage may have to</p>	<p><b>Type of substance</b></p> <p>Low molecular weight substance (oxazolidine derivative)</p>
	<p><b>Administration form</b></p> <p>Tablets, once daily</p>
	<p><b>Targeted acute indications</b></p> <ul style="list-style-type: none"> <li>▪ Prevention of venous thromboembolism following major orthopedic surgery, such as hip and knee replacements</li> </ul>
	<p><b>Targeted chronic indications</b></p> <ul style="list-style-type: none"> <li>▪ Stroke prevention in patients with atrial fibrillation</li> <li>▪ Treatment of deep vein thrombosis</li> <li>▪ Prevention of major cardiovascular events in patients with acute coronary syndrome (ACS)</li> </ul>
	<p><b>Mode of action</b></p> <p>Inhibition of Factor Xa to control the generation of thrombin (an enzyme that facilitates clotting)</p>

be adjusted frequently.

Approximately 6.5 million people worldwide are affected by venous thromboembolism every year. In the United States alone, almost 300,000 people die each year as a result of pulmonary embolism.

**About rivaroxaban**

Rivaroxaban is a novel oral, direct Factor Xa inhibitor. It is an anticoagulant (a drug that has the potential to prevent or treat blood clots) in advanced clinical development for the safe and effective prevention and treatment of venous and arterial thrombosis in both the acute and chronic settings.

Rivaroxaban has the opportunity to be a novel anticoagulant therapy because it is intended to provide a safe, effective, oral, once-daily option that can be used in both the hospital and home settings without the need for routine monitoring.

Rivaroxaban is the most studied oral direct Factor Xa inhibitor in development. More than 40,000 patients are expected to be evaluated in total.

Rivaroxaban is being jointly developed by Bayer HealthCare and Johnson & Johnson Pharmaceutical Research & Development, L.L.C.

**The RECORD phase III study program**

Following positive results from four Phase II studies with rivaroxaban, an extensive Phase III study program to investigate the prevention of VTE following major, elective orthopedic surgery was initiated in late 2005. The RECORD program, comprising four studies, stands for **REgulation of Coagulation in major Orthopedic surgery reducing the Risk of Deep vein thrombosis and pulmonary embolism.**

**Status**

- Extensive Phase III study program (RECORD) in the prevention of VTE after orthopedic surgery
  
- Completion of three of the four studies in the RECORD program and publication of results planned for 2007
  
- Application for marketing authorization for the prevention of VTE following major orthopedic surgery planned for late 2007 in Europe, for 2008 in the United States
  
- Extensive phase III study program in chronic indications initiated in late 2006 (stroke prevention in atrial fibrillation and treatment of venous thromboembolism)

More than 10,000 patients have already been enrolled in these studies. The results of RECORD 3, the first completed study, will be presented on July 8, 2007 at the XXI ISTH (International Society on Thrombosis and Haemostasis) congress during the late-breaking clinical trial results session.

The first application for marketing authorization in the prevention of VTE following major orthopedic surgery is planned for the end of 2007 in Europe and for 2008 in the United States.

**Phase III study program in chronic indications**

At the end of 2006, Bayer HealthCare and Ortho-McNeil announced the start of a wide-ranging phase III study program with rivaroxaban in chronic indications.

The prevention of stroke in patients with atrial fibrillation is the most significant indication in this development program, and one in which there is a very high level of unmet medical need.

In the second chronic indication, treatment of venous thromboembolism, the development program consists of three studies in patients with acute deep vein thrombosis and pulmonary embolism. Most anticoagulant drugs are currently available only in subcutaneous form, and are therefore less suitable for long-term therapy. The only oral anticoagulants currently available are vitamin K antagonists, which require frequent laboratory monitoring and also interact with numerous foods and drugs. This is why rivaroxaban is a promising drug candidate for both prevention and treatment in acute and chronic settings, from hospital to home.

**Collaborating clinical development partner**

Johnson & Johnson  
Pharmaceutical Research  
& Development, L.L.C.

### **Bayer HealthCare**

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 and as Bayer HealthCare Pharmaceuticals in the US and Canada. Bayer HealthCare's aim is to discover and manufacture products that will improve human and animal health worldwide.

### **Bayer Schering Pharma**

Bayer Schering Pharma is a worldwide leading specialty pharmaceutical company. Its research and business activities are focused on the following areas: Diagnostic Imaging, Hematology/Cardiology, Oncology, Primary Care, Specialized Therapeutics 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.

### **Research and Development at Bayer Schering Pharma**

Bayer Schering Pharma concentrates its R&D activities on innovative treatment approaches for diseases with a high unmet medical need to improve patients' quality of life and prolong lives. In this context, Bayer Schering Pharma focuses on its core competencies and its many years of experience. Thus, Bayer Schering Pharma holds a leading position in many therapeutic fields: for example, in the treatment of hemophilia and multiple sclerosis, in contrast media and oral contraception. We are also striving for a leading position in oncology. With new approaches in cancer therapy, for cardiovascular diseases, gynaecological therapies and in molecular imaging, Bayer Schering Pharma aims to become an innovation leader in these fields. In addition, Bayer Schering Pharma further develops products already on the market in order to improve their application and/or extend their range of indications.

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**Forward-looking statements**

This information contains forward-looking statements based on current assumptions and forecasts made by Bayer Group 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 our public reports filed with the Frankfurt Stock Exchange and with the U.S. Securities and Exchange Commission (including Form 20-F). The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.