



## News Release

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Media Contacts: Ian McConnell  
+1 (973) 901-5722

Paul Laland  
(Portola Pharmaceuticals)  
+1 (415) 519-6610

Investor Contacts: Carol Ferguson  
+1 (908) 423-4465

Joe Romanelli  
+1 (908) 423-5088

### **Portola Pharmaceuticals and Merck Announce that Phase 2 Study Showed Investigational Factor Xa Inhibitor, Betrixaban, Reduced Incidence of Bleeding Compared to Warfarin in Patients with Atrial Fibrillation**

ATLANTA, Ga. March 15, 2010 – Portola Pharmaceuticals and Merck today announced the results of EXPLORE-Xa, a Phase 2 exploratory, dose finding study of betrixaban, an investigational oral direct Factor Xa inhibitor. Results showed that a once-daily dose of oral betrixaban, given to patients with non-valvular atrial fibrillation or atrial flutter and at least one risk factor for stroke, reduced the incidence of major and clinically relevant non-major (CRNM) bleeds\* compared to dose-adjusted warfarin. The data were presented during a late-breaking clinical trials session at the American College of Cardiology (ACC) 59<sup>th</sup> Annual Scientific Session in Atlanta.

"Given that bleeding can be a significant safety issue for patients who take warfarin, there is a critical unmet need for anticoagulant therapy options," said U.S. national coordinator in the study, Michael Ezekowitz, MB, ChB, DPhil, vice president of the Lanckenau Institute for Medical Research and professor at Jefferson Medical College. "The EXPLORE-Xa study accomplished its objective of providing important information to guide the betrixaban dosing strategy for future investigational studies."

In this multinational, dose-finding study of 508 patients with non-valvular atrial fibrillation or atrial flutter and at least one risk factor for stroke, a once daily dose of betrixaban 40 mg (n=127) demonstrated significantly less major and CRNM bleeding than open label warfarin (n=127, p=0.035). The risk of major and CRNM bleeding for the 60 mg (n=127) and 80 mg (n=127) doses of betrixaban was similar to warfarin.

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### **About the EXPLORE-Xa Study**

The Phase 2b randomized, parallel group study examined three blinded doses of betrixaban compared with open-label, dose-adjusted warfarin in 508 patients with non-valvular atrial fibrillation or atrial flutter and at least one risk factor for stroke. Patients ranged from ages 46 to 91 and a total of 87 percent previously received a vitamin K antagonist. Participants were not excluded for severe renal impairment, except those on dialysis. One hundred and twenty-seven patients were randomized to each of four treatment groups: betrixaban 40, 60 or 80 mg or open-label warfarin (INR 2-3), the current standard of care. The study was conducted in 35 centers in the U.S., Canada and Germany with a minimum follow-up of three months and a maximum of 12 months. The goal of the study was to assess the safety and tolerability of betrixaban compared to warfarin to provide information to guide further clinical development.

The primary study endpoint was the time to occurrence of major or CRNM bleeding. The incidence (crude rates) of major or CRNM bleeding was 0.8 percent, 3.9 percent, 3.9 percent and 5.5 percent for the betrixaban 40 mg, 60 mg, and 80 mg and warfarin groups, respectively.

The secondary endpoints included the time to occurrence of any bleeding (major, CRNM, and minimal) and the time to occurrence of death, stroke (ischemic or hemorrhagic), myocardial infarction, or other systemic embolism. The incidence (crude rates) of any bleeding was significantly lower compared to warfarin (31.5 percent) for patients taking betrixaban 40 mg (17.3 percent,  $p=0.011$ ) and 80 mg (18.9 percent,  $p=0.022$ ); but not those taking betrixaban 60 mg (25.2 percent,  $p=0.309$ ). The number of events in the secondary composite endpoint of death, stroke, myocardial infarction or other systemic embolism ranged from 0-1 in each of the four dosing groups, which was the expected stroke/embolic event rate for the warfarin control group. There was one stroke each in the betrixaban 60 mg and 80 mg groups, and one death each in the betrixaban 40 mg and warfarin groups. There were no myocardial infarctions or other systemic emboli in any of the four dosing groups.

The most common adverse events in the betrixaban groups combined ( $n=381$ ) were diarrhea (6 percent versus 0.8 percent on warfarin); nausea (5.5 percent versus 1.6 percent on warfarin); constipation (5.2 percent versus 2.4 percent on warfarin); headache (5.2 percent versus 2.4 percent on warfarin) and peripheral edema (6.8 percent versus 7.9 percent on warfarin). A numerically higher percentage of patient discontinuations occurred in each of the three betrixaban groups than in the open label warfarin group (8.7-9.4 percent vs. 6.3 percent).

### **About Merck**

Today's Merck is working to help the world be well. Through our medicines, vaccines, biologic therapies, and consumer and animal products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching programs that donate and deliver our products to the people who need them. Merck. Be Well. For more information, visit [www.merck.com](http://www.merck.com).

### **About Portola Pharmaceuticals, Inc.**

Portola Pharmaceuticals develops innovative therapeutics based on targets with established proofs of concept that are designed to provide significant advances over current treatments for cardiovascular disease and inflammation. The company has global development and commercialization agreements with two of the world's leading pharmaceutical companies collectively valued at about \$1B in upfront and milestone payments plus double-digit royalties on future sales. Betrixaban, its oral direct Factor Xa inhibitor, is licensed to Merck & Co., Inc., and elinorel, its competitive and reversible P2Y<sub>12</sub> ADP receptor antagonist, is licensed to Novartis. Portola's proprietary pipeline programs are focused on the discovery and development of PRT061103, a thromboxane receptor antagonist, which is targeted to address a significant unmet need as a potential aspirin alternative for patients intolerant to aspirin; PRT064445, a Factor Xa inhibitor antidote; and PRT062607, a novel, orally-available Syk-specific kinase inhibitor to treat chronic inflammatory diseases, including rheumatoid arthritis. For additional information, visit [www.portola.com](http://www.portola.com).

### **Forward-Looking Statement**

This news release includes "forward-looking statements" within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. Such statements may include, but are not limited to, statements about the benefits of the merger between Merck and Schering-Plough, including future financial and operating results, the combined company's plans, objectives, expectations and intentions and other statements that are not historical facts. Such statements are based upon the current beliefs and expectations of Merck's management and are subject to significant risks and uncertainties. Actual results may differ from those set forth in the forward-looking statements.

The following factors, among others, could cause actual results to differ from those set forth

in the forward-looking statements: the possibility that the expected synergies from the merger of Merck and Schering-Plough will not be realized, or will not be realized within the expected time period, due to, among other things, the impact of pharmaceutical industry regulation and pending legislation that could affect the pharmaceutical industry; the risk that the businesses will not be integrated successfully; disruption from the merger making it more difficult to maintain business and operational relationships; Merck's ability to accurately predict future market conditions; dependence on the effectiveness of Merck's patents and other protections for innovative products; the risk of new and changing regulation and health policies in the U.S. and internationally and the exposure to litigation and/or regulatory actions.

Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in Merck's 2009 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site ([www.sec.gov](http://www.sec.gov)).

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\* Major bleeding was defined as: a fall in hemoglobin of 2g/dL or more or a transfusion of 2 units of packed cells or whole blood or bleeding at a critical site such as intracranial bleeding.