



# Portola, Bristol-Myers Squibb and Pfizer Sign Clinical Collaboration Agreement to Study ELIQUIS® and Portola's Universal Factor Xa Inhibitor Antidote PRT4445

Thursday, November 01, 2012 - 05:15am

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BUSINESS WIRE)--Portola Pharmaceuticals, Inc., Bristol-Myers Squibb Company (NYSE: BMY) and Pfizer Inc. (NYSE: PFE) today announced a clinical collaboration agreement to conduct a proof-of-concept study of PRT4445 and the investigational oral Factor Xa inhibitor ELIQUIS® (apixaban). PRT4445 is a universal Factor Xa inhibitor antidote in clinical development designed to reverse the anticoagulant activity of any Factor Xa inhibitor. No agents are approved to reverse the activity of Factor Xa inhibitors.

The collaboration will be in effect during the clinical proof-of-concept study, which is anticipated to start by the end of this year. The study is designed to demonstrate the safety of PRT4445 and its ability to reverse the anticoagulation activity of ELIQUIS and other Factor Xa inhibitors, including betrixaban, Portola's Phase 3 oral Factor Xa inhibitor. Bristol-Myers Squibb and Pfizer will make an undisclosed cash payment to Portola upon initiation of the proof-of-concept study with ELIQUIS and will provide development and regulatory guidance for the study. Portola retains 100 percent global development and commercialization rights for PRT4445.

"Oral Factor Xa inhibitors address an important unmet need for patients requiring anticoagulant therapy, but as with all anticoagulants, there is a need for an antidote to

help manage the concerns physicians have around infrequent but serious bleeding events.” said William Lis, chief executive officer of Portola. “This clinical collaboration brings together world-class expertise in the field of thrombosis from Bristol-Myers Squibb, Pfizer and Portola with the goal of accelerating the development of PRT4445 as an antidote to ELIQUIS, while allowing Portola to retain all rights to develop and commercialize the compound in the future.”

“Patient safety and improved patient outcomes have guided our clinical development program for ELIQUIS, including our efforts to identify a reversal agent for urgent clinical situations,” said Brian Daniels, senior vice president, Global Development and Medical Affairs, Bristol-Myers Squibb. “With our partner Pfizer, we look forward to working with Portola to advance the scientific understanding of the role of PRT4445 as a potential antidote for ELIQUIS.”

Major bleeding events occur infrequently in patients taking Factor Xa inhibitors (1-4% per year in clinical studies) and standard measures are employed to manage these events. Development of an agent specifically designed to reverse the activity of Factor Xa inhibitors may provide an antidote for patients who, in rare instances, experience an uncontrolled major bleeding event or require emergency surgery.

#### About PRT4445

PRT4445 is a novel recombinant protein being developed to address serious, uncontrolled bleeding by reversing the anticoagulant activity of Factor Xa inhibitors and low molecular weight heparins in Factor Xa inhibitor-treated patients experiencing uncontrolled major bleeding or requiring emergency surgery. PRT4445 is a modified version of human Factor Xa designed to sequester direct inhibitors (apixaban, betrixaban, rivaroxaban), thereby allowing native Factor Xa to restore hemostasis. In addition, PRT4445 can reduce the Xa inhibition properties of anti-thrombin dependent inhibitors.

Portola has presented nonclinical data on PRT4445 at multiple major scientific conferences and has shown reductions in bleeding in animal models with enoxaparin, fondaparinux and rivaroxaban. Additional in vivo and in vitro data have shown that PRT4445 has the potential to act as a universal antidote for the class of direct Factor Xa inhibitors.

#### About ELIQUIS

ELIQUIS is the approved trade name for apixaban in Europe and the proposed trade name in the U.S. ELIQUIS is not approved for the prevention of stroke or systemic embolism in

patients with atrial fibrillation in any country. In May 2011, Bristol-Myers Squibb and Pfizer announced the first regulatory approval for ELIQUIS in the 27 countries of the European Union plus Iceland and Norway for the prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery.

Bristol-Myers Squibb and Pfizer continue to progress the ELIQUIS application for stroke prevention in atrial fibrillation based on the ARISTOTLE and AVERROES studies. On September 21, 2012, Bristol-Myers Squibb and Pfizer Inc. announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending that ELIQUIS be granted approval for the prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation and with one or more risk factors for stroke. On September 26, 2012, The U.S. Food and Drug Administration (FDA) acknowledged receipt of the ELIQUIS (apixaban) New Drug Application (NDA) resubmission to reduce the risk of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation. The FDA has deemed the resubmission a complete response to its June 22, 2012 Complete Response Letter (CRL) that requested additional information on data management and verification from the ARISTOTLE trial. The FDA Prescription Drug User Fee Act (PDUFA) date is March 17, 2013.

ELIQUIS is also being investigated in Phase 3 trials for the treatment of VTE.

About Portola Pharmaceuticals, Inc.

Portola Pharmaceuticals discovers and develops innovative therapeutics based on targets with established proof of concept that are designed to provide significant advances over current treatments for thrombosis, inflammatory disease and cancer. In thrombosis, Portola is developing betrixaban, a novel, oral, once-daily Factor Xa inhibitor in the global, pivotal Phase 3 APEX Study for hospital and post-discharge prevention of venous thromboembolism (VTE) in acute medically ill patients, and PRT4445, a universal Factor Xa inhibitor antidote which Portola plans to market with betrixaban. In inflammation, Portola is developing highly selective, novel oral Syk inhibitors for the treatment of various autoimmune and inflammatory diseases and novel dual inhibitors of Syk and Janus Kinase (JAK) for hematologic cancers and autoimmune diseases. For additional information, visit [www.portola.com](http://www.portola.com).

About the Bristol-Myers Squibb/Pfizer Collaboration

In 2007, Pfizer and Bristol-Myers Squibb entered into a worldwide collaboration to develop and commercialize ELIQUIS, an investigational oral anticoagulant discovered by Bristol-

Myers Squibb. This global alliance combines Bristol-Myers Squibb's long-standing strengths in cardiovascular drug development and commercialization with Pfizer's global scale and expertise in this field.

#### About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information, please visit <http://www.bms.com> or follow us on Twitter at <http://twitter.com/bmsnews>.

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At Pfizer, we apply science and our global resources to improve health and well-being at every stage of life. We strive to set the standard for quality, safety and value in the discovery, development and manufacturing of medicines for people [and animals]. Our diversified global health care portfolio includes human [and animal] biologic and small molecule medicines and vaccines, as well as nutritional products and many of the world's best-known consumer products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as the world's leading biopharmaceutical company, we also collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. To learn more about our commitments, please visit us at <http://www.pfizer.com>.

#### Bristol-Myers Squibb Forward-Looking Statement

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding product development. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2011, in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-

looking statement, whether as a result of new information, future events or otherwise.

## Pfizer Disclosure Notice

The information contained in this release is as of November 1, 2012. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about various potential indications for ELIQUIS (apixaban), including their potential benefits, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, (i) the uncertainties inherent in research and development; (ii) the companies' ability to address the comments in the complete response letter (CRL) from the Food and Drug Administration expeditiously and to the satisfaction of the FDA; (iii) decisions by the FDA and regulatory authorities in other jurisdictions regarding whether and when to approve drug applications that have been or may be filed for any such indications as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of any such indications; and (iv) competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2011 and in its reports on Form 10-Q and Form 8-K.

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Portola Pharmaceuticals Media Contact: Paul Laland, WCG for Portola, 415-946-1071 plaland@wcgworld.com or Portola Pharmaceuticals Investor Contact: Mardi Dier, CFO, Portola, 650-246-7236 ir@portola.com or Bristol-Myers Squibb Media Contact: Laura Hortas, 609-252-4587 laura.hortas@bms.com or Bristol-Myers Squibb Investor Contact: John Elicker, 609-252-4611 john.elicker@bms.com or Pfizer Inc. Media Contact: MacKay Jimeson, 212-733-2324 MacKay.Jimeson@pfizer.com or Pfizer Inc. Investor Contact: Suzanne Harnett, 212-733-8009 Suzanne.Harnett@pfizer.com