Portola Announces Positive Phase 2 Study Results Showing Factor Xa Inhibitor Antidote PRT4445 Reverses Anticoagulant Activity of Eliquis(R)

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Data Presented in Oral Session at 2013 Congress of the International Society on Thrombosis and Haemostasis

AMSTERDAM, THE NETHERLANDS and SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 07/02/13 -- Portola Pharmaceuticals, Inc. (NASDAQ: PTLA) today announced positive pharmacodynamic and safety data from a Phase 2 proof-of-concept study of its investigational Factor Xa inhibitor antidote PRT4445 in healthy volunteers who were administered the Factor Xa inhibitor *Eliquis*® (apixaban). Results showed greater than a 95 percent reversal of the anticoagulant activity of *Eliquis* was achieved within two minutes of intravenously administered high-dose PRT4445, which has a tentatively approved International Nonproprietary Name (INN) of andexanet alfa. In the study, andexanet alfa was well tolerated, with no serious adverse events or immunologic effects observed. The data were presented in an oral session at the XXIV Congress of the International Society on Thrombosis and Haemostasis (ISTH) in Amsterdam by Mark Crowther, M.D., M.Sc., FRCPC, professor of medicine, Department of Medicine, Hematology and Thromboembolism, McMaster University, Hamilton, Ontario.

"Clinicians are gaining expertise with the use of Factor Xa inhibitors, but there is no effective way to reverse or stop the anticoagulation effect of these agents when a patient requires it," said Dr. Crowther. "These are the first Phase 2 data to indicate that a product can reverse the anticoagulation effect of a Factor Xa inhibitor."

Major bleeding events occur infrequently in patients taking Factor Xa inhibitors (1-4 percent per year in several clinical studies involving patients taking a Factor Xa inhibitor on a chronic basis), and standard measures are currently employed to manage these events. However, there is presently no approved antidote or reversal agent that is specifically intended for use against Factor Xa inhibitors. Development of andexanet alfa, specifically designed to reverse the activity of Factor Xa inhibitors, may provide an antidote for patients who experience an uncontrolled major bleeding event or require emergency surgery.

Portola entered into a collaboration agreement with Bristol-Myers Squibb Company and Pfizer Inc. to study andexanet alfa with *Eliquis* in the Phase 2 study. This is the first in a series of Phase 2 studies that are evaluating the safety and pharmacodynamic activity of andexanet alfa in healthy volunteers who have been administered one of several Factor Xa inhibitors. Portola is currently evaluating andexanet alfa and XARELTO® (rivaroxaban) in a separate Phase 2 study and expects to complete that evaluation in 2013.

"The lack of an effective antidote is restricting the use of Factor Xa inhibitors to patients at low risk for bleeding or requiring surgery. Leading clinicians have identified an antidote as a significant unmet clinical need," said John T. Curnutte, M.D. Ph.D., executive vice president of research and development for Portola. "Based on this need and our data, we believe that andexanet alfa may be granted an accelerated development pathway and we are working closely with the FDA to advance this program as quickly as possible."

Phase 2 Study Design and Results

In the randomized, placebo-controlled, double-blind, cohort dose-escalation Phase 2 study, 27 healthy volunteers were treated on days 1-6 with *Eliquis* 5 mg twice a day (to steady state) and then randomized in a 6:3 ratio to intravenous andexanet alfa (in three different dose cohorts -- 90 mg, 210 mg or 420 mg) or saline on day 6, three hours after receiving the last *Eliquis* dose. Pharmacodynamic and safety data were collected through day 48 and pharmacokinetic data through day 10.

Results demonstrated a dose-dependent reversal of the anticoagulant activity of *Eliquis.* Two minutes after administration of 420 mg andexanet alfa (n=6), the anticoagulant activity of *Eliquis* decreased by greater than 95 percent as measured by anti-Factor Xa activity. Similarly, the 210 mg dose reduced anti-Factor Xa activity by 80 percent compared with saline (n=9). The reversal of anti-Factor Xa activity correlated with a reduction in the level of free, unbound *Eliquis* in the plasma consistent with the mechanism of action of andexanet alfa.

Safety data for all 27 healthy volunteers after 48 days of follow-up showed no thrombotic events, serious adverse events or premature discontinuations of andexanet alfa. The incidence of adverse events with andexanet alfa was similar to that with the control. No antibodies were generated against andexanet alfa, endogenous Factor Xa or Factor X.

About Andexanet Alfa

Andexanet alfa is a novel recombinant protein designed to reverse the anticoagulant activity in patients treated with a Factor Xa inhibitor who suffer an uncontrolled bleeding episode or need to undergo emergency surgery. Andexanet alfa is similar to native Factor Xa, but has been modified to restrict its biological activity to the reversal of the anticoagulant effects of Factor Xa inhibitors. Andexanet alfa acts as a Factor Xa decoy that binds and sequestors direct Factor Xa inhibitors in the blood. Once bound to andexanet alfa, the Factor Xa inhibitors are unable to bind to and inhibit native Factor Xa. The native Factor Xa is then available to participate in the coagulation process and restore hemostasis. Results from a Phase 1 single ascending dose safety and tolerability study of andexanet alfa conducted by Portola in 32 healthy volunteers showed no apparent safety signals,

including no thrombotic adverse events and no antibodies against andexanet alfa, endogenous Factor Xa or Factor X.

About Portola Pharmaceuticals, Inc.
Portola is a biopharmaceutical company focused on the development and commercialization of novel therapeutics in the areas of thrombosis (blood clots), other hematologic disorders and inflammation for patients who currently have limited or no approved treatment options. Portola's current development-stage portfolio consists of three compounds discovered through its internal research efforts and one discovered by Portola scientists during their time at a prior company.

Portola's two lead programs address significant unmet medical needs in the area of thrombosis.

Portola's lead compound, betrixaban, is an investigational, novel, oral, once-daily inhibitor of Factor Xa in Phase 3 development for extended duration prophylaxis (preventive treatment) of a form of thrombosis known as venous thromboembolism (VTE) in acute medically ill patients. Currently, there is no anticoagulant approved for extended duration VTE prophylaxis in this population.

Portola's second lead development candidate, andexanet alfa, is a recombinant protein designed to reverse the anticoagulant activity in patients treated with a Factor Xa inhibitor who suffer an uncontrolled bleeding episode or require emergency surgery. Portola has entered into collaboration agreements with Bristol-Myers Squibb Company and Pfizer Inc., with Bayer Pharma AG and Janssen Pharmaceuticals, Inc., and with Daiichi Sankyo to study andexanet alfa with *Eliquis*® (apixaban), XARELTO® (rivaroxaban) and edoxaban, respectively, in Portola's Phase 2 studies. Portola retains full, worldwide commercial rights with respect to andexanet alfa.

Portola's third product candidate, PRT2070, is an orally available kinase inhibitor being developed for hematologic (blood) cancers and inflammatory disorders. PRT2070 inhibits spleen tyrosine kinase (Syk) and janus kinases (JAK), enzymes that regulate important signaling pathways. Portola plans to file an Investigational New Drug (IND) application in the third quarter of 2013and initiate a Phase 1/2 clinical study of PRT2070 in 2013 in patients with B-cell hematologic cancers who have failed or relapsed on existing marketed therapies or products in development, including patients with identified mutations. Portola's fourth program, PRT2607 and other highly selective Syk inhibitors, is partnered with Biogen Idec Inc.

Forward-looking statement
Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding the use of betrixaban as a Factor Xa inhibitor, the use of PRT4445, which has a tentatively approved International Nonproprietary Name (INN) of andexanet alfa, to reverse the anticoagulant activity in patients treated with a Factor Xa inhibitor, the use of PRT2070 or PRT2607 as kinase inhibitors and any of Portola's clinical trials, including Portola's Phase 3 APEX study for betrixaban, Phase 2 proof-of-concept studies for PRT4445 and Phase1/2 study for PRT2070. Risks that contribute to the uncertain nature of the forward-looking statements include: the accuracy of Portola's estimates regarding its ability to initiate and/or complete its clinical trials; the success of Portola's clinical trials and the demonstrated efficacy of Portola's product candidates thereunder; the accuracy of Portola's estimates regarding its expenses and capital requirements; regulatory developments in the United States and foreign countries; Portola's ability to obtain and maintain intellectual property protection for its product candidates; and the loss of key scientific or management personnel. These and other risks and uncertainties are described more fully in Portola's filings with the Securities and Exchange Commission, including without limitation its Registration Statement on Form S-1 that was originally filed with the Securities and Exchange Commission on April 12, 2013, and the amendments thereto. All forward-looking statements contained in this press release speak only as of the date on which they were made. Portola undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Eliquis is a registered trademark of Bristol-Myers Squibb Company.