



Portola, Bristol-Myers Squibb and Pfizer Announce Statistically Significant Results From the First Part of the Phase 3 ANNEXA(TM)-A Studies of Investigational Andexanet Alfa With Eliquis (apixaban)

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Andexanet Alfa Rapidly Reversed the Anticoagulant Effect of the Factor Xa Inhibitor Eliquis (apixaban) Among All Study Participants - - - Data Presented Today during American Heart Association 2014 Scientific Sessions: "Clinical Science: Special Reports" Session

Portola Pharmaceuticals (NASDAQ: PTLA), Bristol-Myers Squibb Company (NYSE: BMY) and Pfizer Inc. (NYSE: PFE) today announced results from the first part of the Phase 3 ANNEXA™ -A (Andexanet Alfa a Novel Antidote to the Anticoagulant Effects of fXA Inhibitors - Apixaban) studies. Andexanet alfa produced rapid and nearly complete reversal (by approximately 94 percent, p value <0.0001) of the anticoagulant effect of Eliquis (apixaban) in healthy volunteers ages 50-75. The full data set will be presented today in an oral presentation during the "Clinical Science: Special Reports" session at the American Heart Association (AHA) 2014 Scientific Sessions in Chicago, IL.

This first part of the Phase 3 ANNEXA-A trial achieved all of its primary and secondary endpoints with statistical significance (p value <0.0001). The trial included 33 subjects,

with 24 randomized to andexanet alfa and nine to placebo. In the study, two to five minutes after completion of a bolus dose of andexanet alfa, the anticoagulant activity of Eliquis was reversed by approximately 94 percent (p value <0.0001) compared with placebo as measured by anti-Factor Xa activity. Every subject treated with andexanet alfa had between 90 and 96 percent reversal of the anticoagulant activity of Eliquis. The reversal of anti-Factor Xa activity correlated with a significant reduction in the level of free, unbound Eliquis in the plasma, consistent with the mechanism of action of andexanet alfa. Additionally, andexanet alfa restored thrombin generation to baseline normal levels (prior to Eliquis therapy). In this study, no serious adverse events, thrombotic events, or antibodies to Factor X or Xa were reported following andexanet alfa administration. Mild infusion reaction was reported in three subjects.

“The statistically significant reversal of the anticoagulant effect of Eliquis demonstrated in all subjects receiving andexanet alfa, an FDA-designated breakthrough therapy, reinforces our commitment to bring this antidote to market as quickly as possible under an Accelerated Approval pathway,” said John T. Curnutte, M.D., Ph.D., executive vice president, research and development for Portola. “Andexanet alfa is unique. Andexanet alfa rapidly reversed Anti-Xa activity with high specificity and a well-understood mechanism of action. We believe andexanet alfa could be the first universal Factor Xa inhibitor antidote available for anticoagulated patients who are experiencing a major bleeding event or those needing emergency surgery.”

“Bristol-Myers Squibb and Pfizer’s collaboration with Portola for the development and evaluation of andexanet alfa with Eliquis further demonstrates our commitment to delivering innovative therapies,” said Dr. Steven Romano, senior vice president and head, Medicines Development Group, Pfizer Global Innovative Pharmaceutical Business. “We are pleased with the positive results of this ANNEXA-A study, which demonstrated a rapid and near complete reversal of the anticoagulant effects of Eliquis. We look forward to the completion of the second part of this study.”

“Eliquis has proven to be an important treatment option for patients at risk for blood clots due to nonvalvular atrial fibrillation and venous thromboembolism,” said Douglas Manion, M.D., head of specialty development, Bristol-Myers Squibb. “Currently, there is no antidote to Eliquis. Andexanet alfa has the potential to be an effective option for patients who may require reversal of the anticoagulation effects of Eliquis.”

ANNEXA-A Study Design

The randomized, double-blind, placebo-controlled Phase 3 ANNEXA-A study is evaluating the safety and efficacy of andexanet alfa in reversing Eliquis-induced anticoagulation in older healthy volunteers ages 50-75. Efficacy is being evaluated using biomarker endpoints, including anti-Factor Xa levels as the primary endpoint. Secondary endpoints include levels of plasma unbound (free fraction) of Eliquis and thrombin generation levels.

In the first part of the ANNEXA-A study, reported today, 33 healthy volunteers (ages 50-73) were given Eliquis 5 mg twice daily for four days and then randomized in a 3:1 ratio to andexanet alfa administered as a 400 mg IV bolus (n=24) or to placebo (n=9). In the second part, 32 healthy volunteers will be given Eliquis 5 mg twice daily for four days and then randomized in a 3:1 ratio to andexanet alfa administered as a 400 mg IV bolus followed by a continuous infusion of 4 mg/min for 120 minutes or to placebo. Data from the second study are expected in early 2015.

Addressing the Absence of a Factor Xa Inhibitor Antidote

Currently, millions of patients are treated with Factor Xa inhibitors for short-term use or chronic conditions, and the anticoagulant market is expected to continue to grow. Recent patient data[i] confirm earlier clinical trial results showing that, annually, between 1-4 percent of patients treated with Factor Xa inhibitors may experience major bleeding and an additional 1 percent may require emergency surgery. Development of a specific antidote designed to reverse the anticoagulant activity of Factor Xa inhibitors may provide an important treatment option for patients who experience a major bleeding event or require emergency surgery.

About Andexanet Alfa

Andexanet alfa, an FDA-designated breakthrough therapy, is a first-in-class recombinant, modified Factor Xa molecule. It is being developed as an antidote for patients receiving a Factor Xa inhibitor who suffer a major bleeding episode or who may require emergency surgery. Andexanet alfa acts as a Factor Xa decoy that targets and sequesters with high specificity both direct and indirect Factor Xa inhibitors in the blood. Once bound, the Factor Xa inhibitors are unable to bind to and inhibit native Factor Xa, thus allowing for the restoration of normal hemostatic processes. Andexanet alfa has the potential to address numerous clinical scenarios by allowing for flexible and controlled reversal, which can be short-acting through the administration of an IV bolus or longer-acting with the addition of an extended infusion.

About the Andexanet Alfa Clinical Development Program

Portola is evaluating andexanet alfa in randomized, placebo-controlled Phase 3 ANNEXA™ (Andexanet Alfa a Novel Antidote to the Anticoagulant Effects of fXA Inhibitors) registration studies using pharmacodynamic endpoints agreed to with the FDA, such as anti-Factor Xa activity, to demonstrate efficacy. These studies are designed to support the Company's BLA filing for Accelerated Approval. As part of the Accelerated Approval process, a Phase 3b/4 confirmatory patient study evaluating clinical outcomes with andexanet alfa is planned and will be initiated prior to the BLA filing.

Results from four separate Phase 2 proof-of concept studies in healthy volunteers demonstrated that andexanet alfa immediately reversed the anticoagulation activity of four different Factor Xa inhibitors and that the reversal could be sustained. Andexanet alfa has been shown to be well tolerated in Phase 1 and 2 clinical studies, which have included more than 100 healthy volunteers, with no thrombotic events or antibodies to Factor Xa or Factor X observed.

About Eliquis

Eliquis (apixaban) is an oral selective Factor Xa inhibitor. By inhibiting Factor Xa, a key blood-clotting protein, Eliquis decreases thrombin generation and blood clot formation. Eliquis is approved for multiple indications in the U.S. based on efficacy and safety data, including results from seven Phase 3 clinical trials. Eliquis is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation; for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery; for the treatment of DVT and PE; and to reduce the risk of recurrent DVT and PE following initial therapy.

ELIQUIS Important Safety Information

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

(A) Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

(B) Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

use of indwelling epidural catheters concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants a history of traumatic or repeated epidural or spinal punctures a history of spinal deformity or spinal surgery optimal timing between the administration of ELIQUIS and neuraxial procedures is not known

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated.

CONTRAINDICATIONS

Active pathological bleeding Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions)

WARNINGS AND PRECAUTIONS

Increased Risk of Thrombotic Events after Premature Discontinuation: Premature discontinuation of any oral anticoagulant, including ELIQUIS, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant. Bleeding Risk: ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal bleeding. Concomitant use of drugs affecting hemostasis increases the risk of bleeding including aspirin and other anti-platelet agents, other

anticoagulants, heparin, thrombolytic agents, SSRIs, SNRIs, and NSAIDs. Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage. There is no established way to reverse the anticoagulant effect of apixaban, which can be expected to persist for at least 24 hours after the last dose (i.e., about two half-lives). A specific antidote for ELIQUIS is not available. Spinal/Epidural Anesthesia or Puncture: Patients treated with Eliquis undergoing spinal/epidural anesthesia or puncture may develop an epidural or spinal hematoma which can result in long-term or permanent paralysis.

The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic puncture occurs, delay the administration of ELIQUIS for 48 hours.

Monitor patients frequently and if neurological compromise is noted, urgent diagnosis and treatment is necessary. Physicians should consider the potential benefit versus the risk of neuraxial intervention in Eliquis patients.

Prosthetic Heart Valves: The safety and efficacy of ELIQUIS have not been studied in patients with prosthetic heart valves and is not recommended in these patients. Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy: Initiation of ELIQUIS is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.

ADVERSE REACTIONS

The most common and most serious adverse reactions reported with ELIQUIS were related to bleeding.

TEMPORARY INTERRUPTION FOR SURGERY AND OTHER INTERVENTIONS

ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be noncritical in location and easily controlled. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should

be restarted after the surgical or other procedures as soon as adequate hemostasis has been established.

DRUG INTERACTIONS

Strong Dual Inhibitors of CYP3A4 and P-gp: Inhibitors of CYP3A4 and P-gp increase exposure to apixaban and increase the risk of bleeding. For patients receiving ELIQUIS doses greater than 2.5 mg twice daily, the dose of ELIQUIS should be decreased by 50% when it is coadministered with drugs that are strong dual inhibitors of CYP3A4 and P-gp (e.g., ketoconazole, itraconazole, ritonavir, or clarithromycin). For patients receiving ELIQUIS at a dose of 2.5 mg twice daily, avoid coadministration with strong dual inhibitors of CYP3A4 and P-gp. **Strong Dual Inducers of CYP3A4 and P-gp:** Avoid concomitant use of ELIQUIS with strong dual inducers of CYP3A4 and P-gp (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban and increase the risk of stroke and other thromboembolic events. **Anticoagulants and Antiplatelet Agents:** Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding. APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo.

PREGNANCY CATEGORY B

There are no adequate and well-controlled studies of ELIQUIS in pregnant women. Treatment is likely to increase the risk of hemorrhage during pregnancy and delivery. ELIQUIS should be used during pregnancy only if the potential benefit outweighs the potential risk to the mother and fetus.

Please see full Prescribing Information, including **BOXED WARNINGS** and Medication Guide, available at www.bms.com.

About Portola Pharmaceuticals, Inc.

Portola Pharmaceuticals is a biopharmaceutical company developing product candidates that could significantly advance the fields of thrombosis and other hematologic diseases. The Company is advancing its three wholly-owned programs using novel biomarker and genetic approaches that may increase the likelihood of clinical, regulatory and commercial success of its potentially life-saving therapies. Portola's partnered program is focused on developing selective Syk inhibitors for inflammatory conditions.

Betrixaban

Portola's wholly-owned, oral, once-daily Factor Xa inhibitor betrixaban is being evaluated in the only biomarker-based Phase 3 study for hospital-to-home prophylaxis of venous thromboembolism (VTE) in acute medically ill patients. Betrixaban's distinct properties may have the potential to allow the agent to demonstrate efficacy without the significant increase in the rate of major bleeding that was seen in this patient population with other Factor Xa inhibitors. If approved, betrixaban could be the first anticoagulant for both hospital and post-discharge VTE prophylaxis and the standard of care in this large market of more than 20 million patients in the G7 countries alone.

Andexanet Alfa

Andexanet alfa, a recombinant modified human Factor Xa molecule, has the potential to be a first-in-class antidote to reverse the effects of Factor Xa inhibitors in patients who suffer a major bleeding episode or who require emergency surgery. Andexanet alfa has been designated as a breakthrough therapy by the FDA. Portola has entered into Phase 3 clinical collaboration agreements with all of the manufacturers of direct Factor Xa inhibitors while retaining all commercial rights to andexanet alfa. The Company is currently evaluating andexanet alfa in the Phase 3 ANNEXA™ (Andexanet Alfa a Novel Antidote to the Anticoagulant Effects of fXA Inhibitors) registration studies.

Cerdulatinib* (PRT2070)

Portola's product candidate in the area of hematologic cancer, cerdulatinib, is an orally available molecule that uniquely inhibits two validated tumor proliferation pathways - spleen tyrosine kinase (Syk) and janus kinase (JAK). It is currently being evaluated in a Phase 1/2a proof-of-concept study in patients with B cell leukemias or lymphomas with a focus on genetically-defined subtypes, as well as in patients who have failed therapy due to relapse or acquired mutations.

For more information, visit www.portola.com and follow the Company on Twitter @Portola_Pharma.

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>.

About Pfizer Inc.: Working together for a healthier world™

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care 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 one of the world's premier innovative biopharmaceutical companies, we 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, please visit us at www.pfizer.com.

Portola 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: Portola's plans for future clinical studies, timing of clinical study results, future regulatory filings and pursuit of an accelerated approval process for andexanet alfa, anticipated growth in the market for anticoagulants, and the potential efficacy, safety and activity of Portola's product candidates. 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; Portola's ability to manufacture andexanet alfa; 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 most recent filings with the Securities and Exchange Commission, including its Annual Report on Form 10-K and most recent Quarterly Report on Form 10-Q. 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.

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, 2013, 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 17, 2014. 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 Eliquis and andexanet alfa, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; whether and when any BLA may be filed for andexanet alfa; whether and when regulatory authorities will approve any such BLA; and 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, 2013 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the SEC and available at www.sec.gov and www.pfizer.com.

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*Cerdulatinib is a proposed International Nonproprietary Name (pINN).

[i] Source: Truven MARKETSCAN® Commercial, Medicare Supplemental and Medicaid Database (12 months ending September 2013).

Portola Media: Joey Fleury, BrewLife, jfleury@brewlife.com, 415.946.1090 Investors:
Alexandra Santos, Portola Pharmaceuticals, ir@portola.com, 650.246.7239 Bristol-Myers
Squibb Media: Danielle Halstrom, danielle.halstrom@bms.com, 609.419.5512 Investors:
Ranya Dajani, ranya.dajani@bms.com, 609.252.5330 Ryan Asay, ryan.asay@bms.com,
609.252.5020 Pfizer Inc. Media: Steven Danehy, steven.danehy@pfizer.com,
212.733.1538 Investors: Ryan Crowe, ryan.crowe@pfizer.com, 212.733.8160