Portola Pharmaceuticals Provides Update on European Marketing Authorization Application for Betrixaban

South San Francisco, Calif., Dec. 12, 2017 (GLOBE NEWSWIRE) -- Portola Pharmaceuticals, Inc.® (Nasdaq:PTLA) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has requested additional information related to the Marketing Authorization Application (MAA) for betrixaban.

The CHMP has provided the Day 195 List of Outstanding Issues (LoOI) to the company with a request for responses during the next available submission window of January 23, 2018. Based on this new timeline, the Company expects the CHMP to issue an opinion later in the first quarter of 2018.

“We have had a productive ongoing dialogue with the CHMP throughout the MAA process and believe the CHMP questions can be addressed with existing clinical data,” said John T. Curnutte, M.D., Ph.D., executive vice president, research and development. “We look forward to continuing to work with the EMA to address the unmet need in Europe for extended duration prophylaxis of venous thromboembolism in acute medically ill patients.”

The MAA for betrixaban includes data from Portola’s pivotal Phase 3 APEX Study, which enrolled 7,513 patients at more than 450 clinical sites worldwide. The APEX study evaluated oral betrixaban for 35 to 42 days compared with injectable enoxaparin for 6 to 14 days followed by placebo in assessing the prevention of venous thromboembolism (VTE) in high-risk acutely ill medical patients.

Results from the APEX Study have been peer-reviewed and published in *The New England Journal of Medicine*[1], *Circulation*[2] and the *American Heart Journal*.[3]

Betrixaban was approved by the U.S. Food and Drug Administration in June 2017 under the trade name Bevyxxa®.

Important U.S. Safety Information for Bevyxxa (betrixaban) capsules

INDICATION
Bevyxxa is indicated for the prophylaxis of venous thromboembolism (VTE) in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE.

LIMITATIONS OF USE
The safety and effectiveness of Bevyxxa have not been established in patients with prosthetic heart valves because this population has not been studied.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: SPINAL/EPIDURAL HEMATOMA
EPIDURAL OR SPINAL HEMATOMAS MAY OCCUR IN PATIENTS TREATED WITH BEVYXXA WHO ARE RECEIVING NEURAXIAL ANESTHESIA OR UNDERGOING SPINAL PUNCTURE. THE RISK OF THESE EVENTS MAY BE INCREASED BY THE USE OF IN-DWELLING EPIDURAL CATHETERS OR THE CONCOMITANT USE OF MEDICAL PRODUCTS AFFECTING HEMOSTASIS. THESE HEMATOMAS MAY RESULT IN LONG-TERM OR PERMANENT PARALYSIS. CONSIDER THESE RISKS WHEN SCHEDULING PATIENTS FOR SPINAL PROCEDURES.

CONTRAINDICATIONS

- Active pathological bleeding

- Severe hypersensitivity reaction to Bevyxxa

WARNINGS AND PRECAUTIONS

Risk of Bleeding

- Bevyxxa increases the risk of bleeding and can cause serious and potentially fatal bleeding
- Concomitant use of drugs affecting hemostasis increases the risk of bleeding. These include aspirin and other antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, and nonsteroidal anti-inflammatory drugs (NSAIDs)
- Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room
- Promptly evaluate any signs or symptoms of blood loss and consider the need for blood replacement
- Discontinue Bevyxxa in patients with active pathological bleeding
- There is no established way to reverse the anticoagulant effect of Bevyxxa, which can be expected to persist for at least 72hours after the last dose
- It is unknown whether hemodialysis removes Bevyxxa
- Protamine sulfate, vitamin K, and tranexamic acid are not expected to reverse the anticoagulant activity of Bevyxxa

Spinal/Epidural Anesthesia or Puncture

- When neuraxial anesthesia (spinal/epidural anesthesia) or spinal/epidural puncture is employed, patients treated with antithrombotic agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma which can result in long-term or permanent paralysis
- Do not remove an epidural catheter earlier than 72hours after the last administration of Bevyxxa. The next Bevyxxa dose is not to be administered earlier than 5hours after the removal of the catheter. If traumatic puncture occurs, delay the administration of Bevyxxa for 72hours
- Monitor patients frequently for signs and symptoms of neurological impairment (e.g.,numbness or weakness of the legs, bowel or bladder dysfunction). If neurological compromise is noted, urgent diagnosis and treatment is necessary
- Prior to neuraxial intervention, consider the potential benefit versus the risk in anticoagulated patients or in patients to be anticoagulated for thromboprophylaxis

Use in Patients with Severe Renal Impairment

- Patients with severe renal impairment (CrCl ≥ 15 to < 30 mL/min computed by Cockcroft-Gault) taking Bevyxxa may have anincreased risk of bleeding events
- Reduce dose of Bevyxxa, monitor patients closely, and promptly evaluate any signs or symptoms of blood loss in these patients

Use in Patients on Concomitant P-glycoprotein (P-gp) Inhibitors

- Patients on concomitant P-gp inhibitors with Bevyxxa may have an increased risk of bleeding
- Reduce dose of Bevyxxa in patients receiving or starting concomitant P-gp inhibitors, monitor patients closely, and promptly evaluate any signs or symptoms of blood loss in these patients
- Avoid use of Bevyxxa in patients with severe renal impairment receiving concomitant P-gp inhibitors

ADVERSE REACTIONS

- The most common adverse reactions with Bevyxxa were related to bleeding (> 5%)

USE IN SPECIFIC POPULATIONS

Hepatic Impairment

- Bevyxxa has not been evaluated in patients with hepatic impairment, because these patients may have intrinsic coagulation abnormalities
- Bevyxxa is not recommended in patients with hepatic impairment

Please see additional Important Safety Information and full Prescribing Information, including the Boxed Warning at Bevyxxa.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's first medicine Bevyxxa® (betrixaban), an oral, once-daily Factor Xa inhibitor, was approved by the U.S. Food and Drug Administration in June 2017. The company is also working to advance two clinical programs for AndexXa™ (andexanet alfa), a recombinant protein designed to reverse the anticoagulant effect in patients treated with an oral or injectable Factor Xa inhibitor; and cerdulatinib, a SYK/JAK inhibitor in development to treat hematologic cancers. Portola's partnered program is focused on developing selective SYK inhibitors for inflammatory conditions. For more information, visit http://www.portola.com and follow the Company on Twitter @Portola_Pharma.

Forward-looking Statements

This announcement contains forward-looking statements, including statements relating to Portola Pharmaceuticals' expectations regarding the anticipated product availability of Bevyxxa. These statements are subject to significant risks and uncertainties and actual results could differ materially from those projected. Portola Pharmaceuticals cautions investors not to place undue reliance on the forward-looking statements contained in this release. These risks and uncertainties include, without limitation, regulatory timing projections and other risks and uncertainties related to regulatory approval for betrixaban in the European Union. Risks and uncertainties relating to Portola Pharmaceuticals and its business can be found in the "Risk Factors" section of Portola Pharmaceuticals' Quarterly Report on Form 10-Q for the third quarter of 2017, which was filed with the SEC on November 9, 2017. Portola Pharmaceuticals undertakes no duty or obligation to update any forward-looking statements contained in this release as a result of new information, future events or changes in Portola Pharmaceuticals' expectations.

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[1]Cohen et al. Extended Thromboprophylaxis with Betrixaban in Acutely Ill Medical Patients. *New England Journal of Medicine*, 1026; 375.6.

[2] Gibson et al. Extended-Duration Betrixaban Reduces the Risk of Stroke Versus Standard-Dose Enoxaparin Among Hospitalized Medically Ill Patients. *Circulation*. 2017; 135(7):648-655.

[3] Gibson et al. The safety and efficacy of full versus reduced-dose betrixaban in the Acute Medically Ill VTE Prevention With Extended-Duration Betrixaban (APEX) trial. *Am Heart J.* 2017; 185:93-100.

Portola Pharmaceuticals, Inc.