



**U.S. FDA Approves Bevyxxa[®] (betrixaban)
First and Only Anticoagulant for Hospital and Extended Duration Prevention of Venous
Thromboembolism (VTE) in Acutely Ill Medical Patients**

--Company to hold conference call/webcast today at 4:30 p.m. ET--

South San Francisco, Calif. (June 23, 2017) – Portola Pharmaceuticals Inc.[®] (Nasdaq: PTLA) today announced the U.S. Food and Drug Administration (FDA) has approved Bevyxxa (betrixaban), the first and only anticoagulant for hospital and extended duration prophylaxis (35 to 42 days) 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.

Bevyxxa, an oral, once-daily Factor Xa inhibitor, was granted a Fast Track designation and approved by the FDA under Priority Review, which is a status given to drugs that may offer significant improvements in treatment or provide a treatment where no adequate therapy exists. Bevyxxa has been approved based on data from Portola's pivotal Phase 3 APEX Study, which enrolled 7,513 patients at more than 450 clinical sites worldwide.

"Bevyxxa represents a major advance for the field of thrombosis. It is the first therapy to demonstrate a reduction in the incidence of VTE in these high-risk patients without a significant increase in major bleeding," said C. Michael Gibson, M.D., APEX Executive Committee Member and Steering Committee Chairman, professor, Harvard Medical School and chairman of the PERFUSE Study Group. "With this approval, we are finally able to help protect these patients from this often fatal, yet preventable condition."

"Our goal as a company is to bring to market important medicines for the benefit of patients," said Bill Lis, Chief Executive Officer of Portola. "Today's approval is the ultimate milestone for Portola. We are grateful to the patients who participated in our trials, the FDA, our academic collaborators and investigators, and, importantly, our dedicated employees who have worked tirelessly to achieve this goal."

Acutely ill medical patients are those hospitalized for serious medical conditions, including heart failure, stroke, infection and pulmonary disease. Because of their underlying disorder and immobilization, they are at increased risk of developing deep vein thrombosis (DVT) and pulmonary embolism (PE) blood clots.

In the G7 countries, an estimated 24 million acutely ill medical patients are hospitalized each year and are at risk of VTE, either while in the hospital or following discharge. More than one million VTE events and 150,000 VTE-related deaths occur annually in acutely ill medical patients in the G7 countries, despite the standard use of injectable enoxaparin and other heparins in the hospital. More than half of VTE events occur after patients are discharged from the hospital. No other anticoagulant, including enoxaparin or any of the marketed oral Factor Xa

inhibitors, is approved for in-hospital and extended-duration VTE prophylaxis in acutely ill medical patients.

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 VTE in high-risk acutely ill medical patients. As detailed in the prescribing information, Bevyxxa efficacy was measured in the modified Intent-to-Treat (mITT) analysis, which includes 7,441 patients assessed by a composite outcome score comprising either the occurrence of asymptomatic proximal DVT or symptomatic DVT, non-fatal PE or VTE-related death. Bevyxxa reduced the incidence of DVT and PE blood clots compared with those taking enoxaparin plus placebo (4.4 percent vs. 6.0 percent; relative risk 0.75, 95 percent CI: 0.61, 0.91) with no significant increase in major bleeding (0.67 percent vs. 0.57 percent). The most frequent reason for treatment discontinuation was bleeding, with an incidence rate for all bleeding episodes of 2.4 percent and 1.2 percent for betrixaban and enoxaparin, respectively.

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

“For the first time, physicians will have a therapy to help reduce VTE in acutely ill medical patients during their transition from hospital to home, which may ultimately help reduce morbidity,” said Alexander (Ander) T. Cohen, M.B.B.S., M.Sc., M.D., FRACP, APEX Co-Principal Investigator and Co-Chairman of the APEX Executive Committee and Consultant Physician at Guy’s and St Thomas’ NHS Foundation.

The timeline on which Portola expects to launch Bevyxxa is between August and November 2017. During this period, Portola will complete salesforce hiring and training, drug manufacturing validation and inventory buildup. For more information regarding the availability of Bevyxxa, please go to www.bevyxxa.com.

In the EU, the European Medicines Agency’s Committee for Human Medicinal Products (CHMP) is reviewing the Marketing Authorization Application for betrixaban under its standard review period.

CONFERENCE CALL

The Portola management team will host a conference call and webcast today, June 23, 2017, to provide more information about Bevyxxa. The live call can be accessed by phone by calling (844) 452-6828 (domestic) or (765) 507-2588 (international) and specifying conference call ID 45842131. The webcast can be accessed live on the Investor Relations section of the Company's website at <http://investors.portola.com>. It will be archived for 30 days following the call.

BEVYXXA INDICATION AND USE

Bevyxxa (betrixaban) is indicated for the prophylaxis of 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.

¹ Cohen, Alexander T., Robert A. Harrington, Samuel Z. Goldhaber, Russell D. Hull, Brian L. Wiens, Alex Gold, Adrian F. Hernandez, and C. Michael Gibson. "Extended Thromboprophylaxis with Betrixaban in Acutely Ill Medical Patients." *New England Journal of Medicine* 375.6 (2016)

The recommended dose of Bevyxxa is an initial single dose of 160 mg starting on day 1, followed by 80 mg once daily taken for 35 to 42 days at the same time each day with food.

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.

IMPORTANT SAFETY INFORMATION FOR BEVYXXA

Warning: Spinal / Epidural Hematoma

Epidural or spinal hematomas may occur in patients treated with betrixaban 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 betrixaban, which can be expected to persist for at least 72 hours after the last dose.

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. An epidural catheter should not be removed earlier than 72 hours after the last administration of Bevyxxa. The next Bevyxxa dose is not to be administered earlier than 5 hours after the removal of the catheter. If traumatic puncture occurs, delay the administration of Bevyxxa for 7 hours. 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.

Use in Patients with Severe Renal Impairment

Patients with severe renal impairment ($\text{CrCl} \geq 15$ to < 30 mL/min computed by Cockcroft-Gault) taking Bevyxxa may have an increased 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, 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 percent).

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.

For additional information and full Prescribing Information for Bevyxxa, please visit <http://www.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 commercial product, Bevyxxa (betrixaban), an oral, once-daily Factor Xa inhibitor anticoagulant, is approved in the United States. Portola is advancing the clinical development of two other compounds, including 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 www.portola.com and follow the Company on Twitter @Portola_Pharma.

Forward-looking Statements

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 results that may be achieved after treatment with Bevyxxa and the timing of the availability of Bevyxxa to physicians and their patients in the United States. Risks that contribute to the uncertain nature of the forward-looking statements include our manufacturers' ability to manufacture Bevyxxa on a commercial scale or scale to increased production and our overall ability to effectively commercialize Bevyxxa. These and other risks and uncertainties are described more fully in our most recent filings with the Securities and Exchange Commission, including our most recent quarterly report on Form 10-Q, which was filed on May 8, 2017. All forward-looking statements contained in this press release speak only as of the date on which they were made. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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