



## **Portola Announces Data Showing Its Anti-Platelet Drug Inhibits Platelets in Clopidogrel (Plavix®) Non-Responders**

*-- Direct-Acting PRT060128 Provides Reversible, High-level Platelet Inhibition with Immediate Onset of Action --*

**NEW ORLEANS AND SOUTH SAN FRANCISCO, CA** -- Nov. 12, 2008 -- Portola Pharmaceuticals, a biopharmaceutical company developing innovative drugs that provide significant advances in cardiovascular and inflammatory diseases, and cancer, today announced new clinical data that demonstrate PRT060128, the Company's novel anti-platelet drug that directly and reversibly inhibits the P2Y<sub>12</sub> ADP receptor, overcomes high platelet reactivity (HPR) in patients who do not respond to clopidogrel (Plavix®). The results [Abstract #5603] were presented at the American Heart Association (AHA) Scientific Sessions 2008 in New Orleans, LA.

Studies show there is substantial variability in patient response to clopidogrel therapy with up to 30% of patients not responding to treatment. Numerous studies link this suboptimal treatment response to poor clinical outcomes.

PRT060128 is the only reversible, direct acting, intravenous (IV) and oral ADP receptor antagonist in clinical development. Inhibiting the P2Y<sub>12</sub> ADP receptor on platelets has been proven to prevent thrombosis and subsequent heart attacks. Portola believes that PRT060128 may provide significant clinical benefit through immediate, high-level platelet inhibition in the acute setting and a seamless transition to predictable, reversible platelet inhibition in the chronic setting.

"Of the millions of cardiac patients treated with clopidogrel anti-platelet therapy every year, a significant portion do not respond, and remain at high risk for major adverse cardiac events," said Paul A. Gurbel, M.D., principal investigator and Director of Cardiovascular Research at the Center for Thrombosis Research at Sinai Hospital, Baltimore, MD. "These results show that this direct-acting anti-platelet agent with a novel mechanism of action may have the potential to fill this significant treatment gap and meet a major unmet need."

### **Clinical Study Details and Results**

In this study, 20 patients were identified with stable coronary artery disease that were treated with chronic clopidogrel (75mg) and aspirin therapy and have HPR. These clopidogrel non-responders were treated with one oral dose of PRT060128 (60mg) at 12 to 16 hours after the previous day's dose of clopidogrel. Platelet aggregation was determined

by ADP and collagen-induced aggregation and pharmacodynamic assays. The mean platelet reactivity was reduced from the highest (non-responder) to lowest (normal responder) tertile, following dosing with PRT060128, and achieved the predefined endpoint. Inhibition of thrombosis was highly significant in these non-responder patients. The oral dose of PRT060128 chosen for this study is at the low end of the dosing range that will be evaluated in Portola's upcoming Phase II study.

"We are encouraged by these clinical results suggesting PRT060128 may be effective and well tolerated in clopidogrel non-responders," said Charles Homcy, M.D., president and chief executive officer of Portola. "This novel agent has immediate, predictable and reversible platelet inhibition that appears to overcome HPR in non-responders and other major limitations of clopidogrel."

Previously conducted clinical trials showed that PRT060128 was well-tolerated without serious adverse events. In addition, PRT060128 showed predictable, dose-dependent platelet inhibition. Portola expects to begin patient enrollment in an 800 patient Phase II study with the IV and oral forms of PRT060128 for prevention of thrombotic events in patients undergoing non-urgent percutaneous coronary interventions (PCI) before the end of this year.

#### **About Portola Pharmaceuticals, Inc.**

Portola Pharmaceuticals develops innovative therapeutics based on targets with established proof of concept that are engineered to provide significant advances over current treatments for cardiovascular and inflammatory diseases and cancer.

Portola's two lead Phase II compounds, betrixaban, an oral Factor Xa inhibitor and PRT060128, an ADP receptor antagonist, target the global multi-billion dollar antithrombotic market. Both product candidates have best-in-class features versus current and novel agents in development and address the hospital, specialty, and chronic care markets. The Company's earlier-stage programs are leveraging its chemistry and kinase expertise to develop specific Syk and JAK inhibitors to treat cancer and inflammatory diseases with broader activity. The company also has a novel anticoagulant antidote program with the potential to help manage the more than 20 million patients expected to be treated with anticoagulants worldwide in the next decade. For additional information, visit [www.portola.com](http://www.portola.com).

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