ANNEXA™-A: A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial, Demonstrating Reversal of Apixaban-Induced Anticoagulation in Older Subjects by Andexanet alfa (PRT064445), a Universal Antidote for Factor Xa (fXa) Inhibitors

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Background: Direct FXa inhibitors appear to have superior anticoagulant efficacy and safety relative to warfarin and low molecular weight heparin. However, they are limited by the lack of a specific antidote to reverse anticoagulation in cases of serious bleeding episodes or prior to urgent/emergency surgery. Andexanet alfa (AnXa, PRT064445) is a modified, recombinant human FXa molecule that is catalytically inactive but retains high-affinity binding to direct and indirect fXa inhibitors. Thus, it acts as a FXa decoy and reverses FXa inhibitor-mediated anticoagulation. We have previously reported randomized Phase 2 data in healthy subjects anticoagulated with apixaban, rivaroxaban, or enoxaparin, where AnXa rapidly and significantly reversed anti-FXa activity and the inhibition of thrombin generation. Here we report data from the first Phase 3 registration study of AnXa administered to older subjects anticoagulated with apixaban.

Methods: ANNEXATM-A is a Phase 3, double-blind, placebo-controlled study of AnXa in older subjects treated with apixaban. Part 1 of the study investigated a bolus regimen and Part 2 will investigate a bolus followed by a 2 hour continuous infusion. In Part 1, 34 subjects age 50 to 75 were randomized to receive either AnXa or placebo in a 3:1 ratio. All subjects received apixaban 5 mg PO BID for 4 days. AnXa at a dose of 400 mg IV bolus or placebo was administered on Day 4, 3 hours after the last apixaban dose (approximate apixaban Cmax). Safety data were collected through Day 43. The primary efficacy endpoint is the reversal of apixaban-induced anti-FXa activity (mean change from baseline at 2 or 5 min after the end of the bolus). Additional efficacy endpoints included reduction in plasma free fraction of apixaban and restoration of thrombin generation.

Results and Conclusions: Part 1 of the pivotal Phase 3 study has been completed. Final efficacy and safety results for Part 1 will be presented and discussed.

Disclosure:
M. Crowther: Speakers Bureau; Modest; Bayer, Celgene, Leo Pharma, Shire. Consultant/Advisory Board; Modest; Leo Pharma. Consultant/Advisory Board; Significant; Portola. G.G. Levy: Employment; Significant; Portola. Ownership Interest; Significant; Portola. G. Lu: Employment; Significant; Portola. Ownership Interest; Significant; Portola. J. Leeds: Employment; Significant; Portola. Ownership Interest;
Significant; Portola. **L. Barron**: Employment; Significant; Portola. Ownership Interest; Significant; Portola. **P.B. Conley**: Employment; Significant; Portola. Ownership Interest; Significant; Portola. **J. Castillo**: Employment; Significant; Portola. Ownership Interest; Significant; Portola. **J.T. Curnutte**: Employment; Significant; Portola. Ownership Interest; Significant; Portola. **S. Connolly**: Research Grant; Significant; Sanofi-Aventis, Bristol-Myers Squibb, Boehringer-Ingelheim, Boston Scientific, St. Jude Medical, Portola Pharmaceutical, Johnson and Johnson. Speakers Bureau; Significant; Sanofi-Aventis, Bristol-Myers Squibb, Boehringer-Ingelheim. Consultant/Advisory Board; Significant; Sanofi-Aventis, Bristol-Myers Squibb, Boehringer-Ingelheim, Bayer Pharmaceuticals Inc.