Portola Investor Room

Portola Pharmaceuticals Announces Results Demonstrating Andexxa® was Associated with Lowest Rate of Mortality in Patients with Multiple Types of Factor Xa Inhibitor-Related Bleeds

Real-World Data Support Use of Andexxa Can Improve Outcomes

SOUTH SAN FRANCISCO, Calif., March 16, 2020 /PRNewswire/ -- Portola Pharmaceuticals, Inc.® (Nasdaq: PTLA) today announced new data reinforcing the value of Andexxa® [coagulation factor Xa (recombinant), inactivated-zhzo], the first and only FDA-approved reversal agent for the Factor Xa inhibitors rivaroxaban or apixaban. The data demonstrated that Andexxa was associated with a lower rate of in-hospital and 30-day mortality in patients with life-threatening Factor Xa inhibitor-related bleeds compared with other treatment options. This included lower mortality across multiple bleed types including intracranial hemorrhage (ICH), gastrointestinal bleeding (GI) and bleeding due to trauma, when compared to 4-factor prothrombin complex concentrate (4F-PCC) therapy, which is approved only for the reversal of warfarin.

"The number of patients experiencing serious, life-threatening bleeding associated with Factor Xa inhibitors continues to increase as their use grows rapidly in the U.S. and Europe," said Craig I. Coleman, Pharm.D., University of Connecticut, School of Pharmacy and Hartford Hospital Evidence-Based Practice Center. "For the first time, we are presenting real-world data that demonstrates that for these patients Andexxa was associated with the lowest in-hospital mortality across a variety of other treatment options."

Key results, originally scheduled to be presented at the American College of Cardiology's Annual Scientific Session together with the World Congress of Cardiology (ACC.20/WCC),* demonstrated:

- Case matched data showed 30-day mortality was 14.6% with Andexxa versus 34.1% with 4F-PCC across all bleed types, a relative risk reduction of 57.2% (abstract #1213-209 / 209).
  - Among the subgroup of patients who experienced ICH, 30-day mortality was lower in the Andexxa group (15.3% vs. 48.9%), and the relative risk reduction was greater (68.7%).

- In a separate analysis, real-world data showed in-hospital mortality was 4% with Andexxa and 10% with 4F-PCC across all bleed types (abstract #1055-05).
  - Among the subset of patients who experienced ICH, the in-hospital mortality was 9% with Andexxa versus 25% with 4F-PCC.

"This important comparison of Andexxa to 4F-PCC demonstrated lower 30-day mortality with the use of Andexxa in patients with Factor Xa inhibitor-related bleeding across multiple types of bleeds," said Alexander T. Cohen, MBBS, M.Sc., M.D., a consultant physician and epidemiologist at Guy's and St Thomas' Hospitals NHS Foundation Trust. "I believe these findings strengthen the case for the use of Andexxa versus 4F-PCC in these patients, and further establish Andexxa as the standard of care for a broad..."
group of patients on rivaroxaban or apixaban who are experiencing life-threatening or uncontrolled bleeding."

The new findings are based on the results of multiple data sets. One analysis provided an indirect comparison of Andexxa and 4F-PCC using case-matched data from two large studies of Factor Xa inhibitor patients – the 322-patient ANNEXA-4 study and ORANGE, a three-year prospective registry of patients admitted to UK hospitals with major bleeding who received 4F-PCC. The second was a real-world study of electronic medical records from 45 U.S. hospitals used to identify patients admitted for bleeding related to Factor Xa inhibitors (1,075 bleeds) and managed with either Andexxa or 4F-PCC.

"These findings contribute to the growing body of evidence supporting the potential life-saving benefits of Andexxa, the first and only FDA-approved reversal agent for the Factor Xa inhibitors rivaroxaban or apixaban," said Rajiv Patni, M.D., Portola's chief medical officer. "We have a robust strategy to generate and present additional data over the next year, which we believe will enhance our ability to educate key hospital stakeholders that by choosing Andexxa, they can prioritize both the clinical value it provides and responsible budgeting in their patient care."

In addition, new health economics and outcomes research (HEOR) data reveal the burden of bleeding requiring hospitalization on patients and healthcare systems. Hospitalization for ICH bleeds was associated with the highest in-patient mortality, the greatest need for further out-of-home care and the longest length of stay in the hospital compared to other bleed types (abstract #1320-233 / 233). The high thrombotic risk profile (e.g., those with atrial fibrillation [AF] or deep vein thrombosis/pulmonary embolism [DVT/PE]) of included patients suggests that many could have been receiving oral anticoagulants.

Data accepted by ACC.20/WCC* includes:

- **Management of Oral Factor Xa Inhibitor Bleeding-Related Hospitalizations with Andexanet Alfa or 4-Factor Prothrombin Complex Concentrate** (*abstract #1055-05*)

  **Presenter:** Craig I. Coleman, Pharm.D., University of Connecticut, School of Pharmacy/Hartford Hospital Evidence-Based Practice Center  
  **Original Format:** Moderated Poster Presentation  
  **Session:** Updates in VTE and Stroke

- **30 Day Mortality Following Andexanet Alfa in ANNEXA-4 Compared with Prothrombin Complex Concentrate (PCC) Therapy in The ORANGE Study for Life-Threatening Non-Vitamin K Oral Anticoagulant (NOAC) Related Bleeding** (*abstract #1213-209 / 209*)

  **Presenter:** Alexander T. Cohen, MBBS, M.Sc., M.D., Guy's and St Thomas' Hospitals NHS Foundation Trust  
  **Original Format:** Poster Presentation
Outcomes Associated with Bleeding-Related Hospitalizations in Patients at High Thrombotic Risk Findings from the Nationwide Readmission Database (abstract #1320-233 / 233)

Presenter: Craig I. Coleman, Pharm.D., University of Connecticut, School of Pharmacy/Hartford Hospital Evidence-Based Practice Center

Important Safety Information

The most frequently reported adverse reactions in clinical trials in healthy subjects with Andexxa were mild or moderate infusion-related reactions comprising symptoms such as flushing and feeling hot (very common), and cough, dysgeusia, and dyspnea (common). Amongst bleeding patients, commonly reported side effects were ischemic stroke and pyrexia, with uncommon reported side effects of cerebral infarction, cerebrovascular accident, transient ischemic attack, acute myocardial infarction, cardiac arrest, myocardial infarction, deep vein thrombosis, iliac artery occlusion, pulmonary embolism.

Please refer to full Prescribing Information for more information, including Boxed Warning, at www.Andexxa.com.

About Portola Pharmaceuticals, Inc.

Portola Pharmaceuticals is a global, commercial-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics that could significantly advance the fields of thrombosis and other hematologic conditions. The Company's first two commercialized products are Andexxa® [coagulation factor Xa (recombinant), inactivated-zhzo], marketed in Europe as Ondexxya® (andexanet alfa), and Bevyxxa® (betrixaban). The company also is advancing cerdulatinib, a SYK/JAK inhibitor being developed for the treatment of hematologic cancers. Founded in 2003 in South San Francisco, California, Portola has operations in the United States and Europe.

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 Portola's development plans, and the potential benefits of Andexxa. Risks that contribute to the uncertain nature of the forward-looking statements include: the risk that physicians, patients and payers may not see the benefits of utilizing Andexxa for the indications for which it is approved; our ability to continue to manufacture our products and to expand approved manufacturing facilities; the possibility of unfavorable results from additional clinical trials or other studies involving Andexxa; our ability to grow our commercial operations in the EU and generate product revenue within projected timelines and budget; the risk that we may not obtain additional regulatory approvals necessary to expand approved indications for Andexxa; our expectation that we will incur losses for the foreseeable future and will need additional funds to finance our operations; the accuracy of our estimates regarding expenses and capital requirements; our ability to successfully build a hospital-based sales force and commercial infrastructure; our ability to obtain and maintain intellectual property protection for our product candidates; our ability to retain key scientific or management personnel and general market conditions. 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 annual report on Form 10-K. 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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https://investors.portola.com/2020-03-16-Portola-Pharmaceuticals-Announces-Results-Demonstrating-Andexxa-R-was-Associated-with-Lowest-Rate-of-Mortality-in-Patients-with-Multiple-Types-of-Factor-Xa-Inhibitor-Related-Bleeds