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Bristol-Myers Squibb and Pfizer to Present New Analyses of Eliquis™ (apixaban) Clinical and Real-World Data at the American College of Cardiology 2017 Scientific Session

Monday, March 06, 2017 - 03:30am

Post-hoc Analyses from the ARISTOTLE Trial Featured in Late-Breaker and Poster Sessions Real-World Data Analyses Include Database Reviews of U.S. Medicare Patient Population

Bristol-Myers Squibb Company (NYSE:BMY) and Pfizer Inc. (NYSE:PFE) today announced that eight abstracts have been accepted for presentation at the American College of Cardiology (ACC) 66th Annual Scientific Session, taking place March 17-19 in Washington, D.C. In addition to post-hoc analyses from the pivotal Phase 3 ARISTOTLE (**A**pixaban for **R**eduction **I**n **ST**roke and **O**ther **T**hromboembo**L**ic **E**vents in Atrial Fibrillation) trial, the Bristol-Myers Squibb and Pfizer Alliance will present real-world data analyses that illustrate the Alliance's ongoing commitment to understanding the use of direct oral anticoagulants, including *Eliquis*™ (apixaban), in routine clinical practice. This real-world research, part of the global ACROPOLIS™ (**A** pixaban Experien**C**e Through **R**eal-W**O**rld **PO**pu**L**at**I**on **S**tudies) program, aims to complement findings from clinical trials and contribute to the growing body of knowledge around anticoagulation.

In a Late-Breaking Clinical Trials session, the Alliance will highlight a post-hoc analysis from the ARISTOTLE trial, titled *ARISTOTLE: Digoxin and Mortality in Patients with Atrial Fibrillation with and without Heart Failure: Does Serum Digoxin Concentration Matter?* Results of the analysis will be presented on March 19 at 11:00 a.m. Eastern Daylight Time.

"During ACC, the Bristol-Myers Squibb and Pfizer Alliance will share several analyses that delve deeper into the robust data generated from the ARISTOTLE study," said Christoph Koenen, M.D., MBA, VP, Development Lead, *Eliquis*, Bristol-Myers Squibb. "Through continued analyses and support of the ARISTOTLE trial, we can examine topics such as outcomes for patients with different comorbidities and the potential treatment effects of interacting drugs, which expands our scientific understanding."

"As physicians evaluate options for reducing stroke risk in patients with non-valvular atrial fibrillation, they often face questions about the effectiveness and safety of therapies in day-to-day practice," said Rory O'Connor, M.D., Chief Medical Officer, Pfizer Innovative Health. "Real-world data analyses allow us to explore the usage of *Eliquis* and anticoagulants across various geographies and subgroups of patients. Alongside clinical data, the real-world data analyses we are presenting during ACC have the potential to help healthcare providers make more informed decisions along with their patients."

Below is a complete list of Bristol-Myers and Pfizer Alliance presentations during ACC. Abstracts can be accessed through the ACC.17 Online Program Planner.

Title	Presenting Author/Type	Date/Time (EDT)	Location/Session
Phase 3 Clinical Trial Post-Hoc Analyses			
ARISTOTLE: Digoxin and Mortality in Patients with Atrial Fibrillation with and without Heart Failure: Does Serum Digoxin Concentration Matter?	Lopes et al./ Late-Breaker	Mar. 19, 11:00 AM	Late-Breaking Clinical Trials, ACC.17 Main Tent, Hall D
Session: Late-Breaking Clinical Trials			
Use of Interacting Drugs Did Not Modify Treatment Effects of Apixaban Versus Warfarin for Atrial Fibrillation: Results from the ARISTOTLE Trial	Washam et al./ Poster	Mar. 18, 9:45 AM	Poster Hall, Hall C
Session: Arrhythmias and Clinical EP: Anticoagulation Issues			
Aortic Stenosis, but Not Mitral or Aortic Regurgitation, Associated with Adverse Outcomes with Atrial Fibrillation: Results from the ARISTOTLE Trial	Wang et al./ Poster	Mar. 18, 3:45 PM	Poster Hall, Hall C
Session: Arrhythmias and Clinical EP: AF Miscellaneous and Surgical Issues			
Real-World Data and Other Analyses			
Effectiveness and Safety of Apixaban, Dabigatran, and Rivaroxaban Compared to Warfarin among Non-Valvular Atrial Fibrillation Patients in the US Medicare Population	Amin et al./ Moderated Poster	Mar. 17, 11:15 AM	Arrhythmias and Clinical EP Moderated Poster Theater, Poster Hall, Hall C
Session: Atrial Fibrillation, Anticoagulation and Novel Device Therapies			

Real World Evaluation of Major Bleeding Risk and Costs for All Causes and Bleeding-related Health Services among Elderly Patients with Nonvalvular Atrial Fibrillation Treated with Apixaban or Warfarin	Deitelzweig et al./ Moderated Poster	Mar. 17, 10:15 AM	Arrhythmias and Clinical EP Moderated Poster Theater, Poster Hall, Hall C
Session: Atrial Fibrillation, Anticoagulation and Novel Device Therapies			
Real-World Comparison of Major Bleeding and Associated Costs among Oral Anticoagulant-naïve Non-valvular Atrial Fibrillation Patients Initiating Apixaban, Dabigatran, Rivaroxaban, or Warfarin in the US Medicare Population	Amin et al./ Poster	Mar. 18, 9:45 AM	Poster Hall, Hall C
Session: Arrhythmias and Clinical EP: Anticoagulation Issues			
Bleeding Risk among Japanese Non-valvular Atrial Fibrillation Patients Initiated on Apixaban, Dabigatran, Rivaroxaban or Warfarin in the Real World	Wang et al./ Poster	Mar. 18, 9:45 AM	Poster Hall, Hall C
Session: Arrhythmias and Clinical EP: Anticoagulation Issues			
What are the Differences in Oral Anticoagulant Treatment Persistence in Non-Valvular Atrial Fibrillation in Europe? Real-World Studies in Three European Countries	Fauchier et al./ Poster	Mar. 18, 3:45 PM	Poster Hall, Hall C
Session: Innovative Approaches for Reducing Risk and Improving Outcomes With Ablation			

About *Eliquis*

Eliquis (apixaban) is an oral selective Factor Xa inhibitor. By inhibiting Factor Xa, a key blood clotting protein, *Eliquis* decreases thrombin generation and blood clot formation. *Eliquis* is approved for multiple indications in the U.S. based on efficacy and safety data from seven Phase 3 clinical trials. *Eliquis* is a prescription medicine indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation

(NVAF); for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery; for the treatment of DVT and PE; and to reduce the risk of recurrent DVT and PE, following initial therapy.

ELIQUIS Important Safety Information

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

(A) Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

(B) Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- **use of indwelling epidural catheters**
- **concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants**
- **a history of traumatic or repeated epidural or spinal punctures**
- **a history of spinal deformity or spinal surgery**
- **optimal timing between the administration of ELIQUIS and neuraxial procedures is not known**

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated.

CONTRAINDICATIONS

- Active pathological bleeding
- Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions)

WARNINGS AND PRECAUTIONS

- **Increased Risk of Thrombotic Events after Premature Discontinuation:** Premature discontinuation of any oral anticoagulant, including ELIQUIS, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.
- **Bleeding Risk:** ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding.
    - Concomitant use of drugs affecting hemostasis increases the risk of bleeding, including aspirin and other antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, SSRIs, SNRIs, and NSAIDs.
    - Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage.

    - There is no established way to reverse the anticoagulant effect of apixaban, which can be expected to persist for at least 24 hours after the last dose (i.e., about two half-lives). A specific antidote for ELIQUIS is not available.
- **Spinal/Epidural Anesthesia or Puncture:** Patients treated with ELIQUIS undergoing spinal/epidural anesthesia or puncture may develop an epidural or spinal hematoma which can result in long-term or permanent paralysis.

  The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic puncture occurs, delay the administration of ELIQUIS for 48 hours.

  Monitor patients frequently and if neurological compromise is noted, urgent diagnosis and treatment is necessary. Physicians should consider the potential benefit versus the risk of neuraxial intervention in ELIQUIS patients.

- **Prosthetic Heart Valves:** The safety and efficacy of ELIQUIS have not been studied in patients with prosthetic heart valves and is not recommended in these patients.
- **Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy:** Initiation of ELIQUIS is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.

ADVERSE REACTIONS

- The most common and most serious adverse reactions reported with ELIQUIS were related to bleeding.

TEMPORARY INTERRUPTION FOR SURGERY AND OTHER INTERVENTIONS

- ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be noncritical in location and easily controlled. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established.

DRUG INTERACTIONS

- **Strong Dual Inhibitors of CYP3A4 and P-gp:** Inhibitors of cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) increase exposure to apixaban and increase the risk of bleeding. For patients receiving ELIQUIS doses of 5 mg or 10 mg twice daily, reduce the dose of ELIQUIS by 50% when ELIQUIS is coadministered with drugs that are strong dual inhibitors of CYP3A4 and P-gp (e.g., ketoconazole, itraconazole, ritonavir, or clarithromycin). In patients already taking 2.5 mg twice daily, avoid coadministration of ELIQUIS with strong dual inhibitors of CYP3A4 and P-gp.
- **Strong Dual Inducers of CYP3A4 and P-gp:** Avoid concomitant use of ELIQUIS with strong dual inducers of CYP3A4 and P-gp (e.g., rifampin, carbamazepine, phenytoin, St. John’s wort) because such drugs will decrease exposure to apixaban and increase the risk of stroke and other thromboembolic events.

- **Anticoagulants and Antiplatelet Agents:** Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding. APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo.

PREGNANCY CATEGORY B

- There are no adequate and well-controlled studies of ELIQUIS in pregnant women. Treatment is likely to increase the risk of hemorrhage during pregnancy and delivery. ELIQUIS should be used during pregnancy only if the potential benefit outweighs the potential risk to the mother and fetus.

Please see full Prescribing Information, including BOXED WARNINGS and Medication Guide, available at www.bms.com.

About ACROPOLIS™

ACROPOLIS™ (**A**pixaban Experien**C**e Through **R**eal-W**O**rld **PO**pu**L**at**I**on **S**tudies) is the *Eliquis* (apixaban) global real-world data program designed to generate additional evidence from routine clinical practice settings to further inform healthcare decision makers, including healthcare providers and payers. The ACROPOLIS program will include retrospective, outcomes-based analyses from over 10 databases around the world, including medical records, medical and pharmacy health insurance claims data, and national health data systems.

Analyses of real-world data allow for a broader understanding of patient outcomes associated with *Eliquis* outside of the clinical trial setting, as well as insight into other measures of healthcare delivery, such as hospitalization and costs.

About ARISTOTLE

ARISTOTLE (**A**pixaban for **R**eduction **I**n **ST**roke and **O**ther **T**hromboembo**L**ic **E**vents in Atrial Fibrillation) was designed to evaluate the efficacy and safety of *Eliquis* versus warfarin for the prevention of stroke or systemic embolism. In ARISTOTLE, 18,201 patients were randomized (9,120 patients to *Eliquis* and 9,081 to warfarin). ARISTOTLE was an active-controlled, randomized, double-blind, multi-national trial in patients with nonvalvular atrial fibrillation or atrial flutter, and at least one additional risk factor for stroke. Patients were randomized to treatment with *Eliquis* 5 mg orally twice daily (or 2.5 mg twice daily in selected patients, representing 4.7 percent of all patients) or warfarin (target INR range 2.0-3.0), and followed for a median of 1.8 years.

About the Bristol-Myers Squibb/Pfizer Collaboration

In 2007, Pfizer and Bristol-Myers Squibb entered into a worldwide collaboration to develop and commercialize apixaban, an oral anticoagulant discovered by Bristol-Myers Squibb. This global alliance combines Bristol-Myers Squibb's long-standing strengths in cardiovascular drug development and commercialization with Pfizer’s global scale and expertise in this field.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb, visit us at BMS.com or follow us on LinkedIn, Twitter, YouTube and Facebook.

About Pfizer Inc.: Working together for a healthier world®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @PfizerNews, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Bristol-Myers Squibb Forward-Looking Statement

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding product development. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2016, in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Pfizer Disclosure Notice

The information contained in this release is as of March 6, 2017. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Eliquis (apixaban), including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including, without limitation, the ability to meet anticipated clinical trial commencement and completion dates as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of Eliquis; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the SEC and available at www.sec.gov and www.pfizer.com.

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