

# Bristol-Myers Squibb-Pfizer Alliance ACROPOLIS™ Real-World Data Program Grows to Sample Size of Nearly One Million Lives Worldwide

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- *New analyses to be presented at ESC Congress 2018 offer additional insights into varied nonvalvular atrial fibrillation patient populations*

[PRINCETON, N.J. & NEW YORK] August 20, 2018 – The Bristol-Myers Squibb-Pfizer Alliance will present 15 Eliquis® (apixaban) posters at the ESC Congress 2018 held in Munich, Germany, August 25- 29, 2018. Nine of the posters to be presented are new analyses from the global real-world data (RWD) program, ACROPOLIS™ (Apixaban ExperienCe Through Real-WOrld POpuLatIon Studies), exploring the effectiveness and safety of anticoagulants, including Eliquis, among patients with non-valvular atrial fibrillation. These data add to the growing body of real-world evidence for Eliquis, which now includes a sample size of more than 970,000 lives.

The analyses that will be presented at the ESC Congress 2018 as part of ACROPOLIS will offer new insights on patients who have non-valvular atrial fibrillation and a range of comorbidities. The analyses explore other important topics such as healthcare costs, including hospitalization due to bleeding.

“There remains a significant need for data on the treatment responses of patients treated with Eliquis, warfarin or other direct oral anticoagulants in routine clinical practice. This includes patients who present with additional risk factors compounding their risk for non-valvular atrial fibrillation-associated stroke,” said Dr. Christoph Koenen, Head of Cardiovascular Development, Bristol-Myers Squibb. “The sample size of nearly one million analyzed through the ACROPOLIS program can help uncover new aspects of the care experience.”

“The real-world evidence generated from data collected in routine medical practice complements the clinical trial data we have for patients treated with Eliquis,” said Dr. Rory O’Connor, Chief Medical Officer, Pfizer Internal Medicine. “The ACROPOLIS program and its continued growth is a pivotal part of the BMS-Pfizer Alliance’s commitment to expanding the body of evidence related to the use of oral anticoagulants.”

The ACROPOLIS program provides a robust source of complementary information to healthcare professionals. The source and type of RWD may limit how results and endpoints can be applied to the overall patient population. RWD are not to be used as stand-alone evidence for healthcare decision making. Please see additional RWD limitations, as well as Indications and Important Safety Information for Eliquis below.

Below is a complete list of Bristol-Myers Squibb- Pfizer Alliance presentations during the ESC Congress 2018. For a full list of poster titles and authors, visit <https://www.escardio.org/Congresses-&-Events/ESC-Congress/Scientific-sessions>.

**Clinical & HEOR Data (all times listed in CET)**

Date	Session Name	Session Type	Time CET	Location
8.25.18	Elevated biomarkers are associated with increased risk of death and heart failure hospitalization in patients with atrial fibrillation: insights from the ARISTOTLE trial (Ziad Hijazi et al./Poster)	Session: Poster Session 1: Atrial fibrillation: epidemiology, prognosis, outcome 2	11:00-16:00	Poster Area
8.25.18	Comparison of effectiveness, safety, and healthcare costs in non-valvular atrial fibrillation patients with heart failure prescribed direct oral anticoagulants (Alessandra Bassalobre Garcia et al./Poster)	Session: Poster Session 1: Atrial fibrillation: epidemiology, prognosis, outcome 2	11:00-16:00	Poster Area
8.26.18	Comparative effectiveness and safety of non-vitamin K agonist oral anticoagulants versus warfarin in non-valvular atrial fibrillation patients: The dose subgroup analysis of the ARISTOPHANES study (Xiaoyan Li et al./Poster)	Session: Poster Session 3: Atrial fibrillation – Stroke prevention – General	14:00-18:00	Poster Area
8.26.18	Comparisons of clinical and economic outcomes between non-VKA oral anticoagulants among non-valvular atrial fibrillation patients: the ARISTOPHANES study (Xiaoyan Li et al./Poster)	Session: Poster Session 3: Health economics	14:00-18:00	Poster Area
8.26.18	Comparative effectiveness and safety between non-VKA oral anticoagulants in non-valvular atrial fibrillation patients: a dose subgroup analysis of the ARISTOPHANES study (Xiaoyan Li et al./Poster)	Session: Poster Session 3: Atrial fibrillation – Stroke prevention	14:00-18:00	Poster Area
8.26.18	Comparisons of clinical and economic outcomes between non-VKA oral anticoagulants and warfarin among non-valvular atrial fibrillation patients: the ARISTOPHANES study (Xiaoyan Li et al./Poster)	Session: Poster Session 3: Health economics	14:00-18:00	Poster Area
8.27.18	Effectiveness, safety, and composite clinical outcomes of apixaban, dabigatran, rivaroxaban, relative to warfarin in non-valvular atrial fibrillation patients in the US Medicare population (Amol Dhamane et al./Poster)	Session: Poster Session 4: Atrial fibrillation – Stroke prevention	8:30-12:30	Poster Area
8.27.18	The comparative safety and effectiveness of antithrombotic treatment in non-valvular atrial fibrillation following a first clinically relevant bleed: an observational study in the United Kingdom (Sreeram Ramagopalan et al./Poster)	Session: Poster Session 4: Atrial fibrillation – Stroke prevention	8:30-12:30	Poster Area
8.27.18	Treatment initiation patterns among newly diagnosed non-valvular atrial fibrillation patients: Insights from a large German claims database (Stefan Hohnloser et al./Poster)	Session: Poster Session 4: Atrial fibrillation – Stroke prevention	8:30-12:30	Poster Area
8.27.18	Effectiveness, safety, and composite clinical outcomes between apixaban and other oral anticoagulants for non-valvular atrial fibrillation patients in the US Medicare population (Amol Dhamane et al./Poster)	Session: Poster Session 5: Atrial fibrillation – Stroke prevention 1	14:00-18:00	Poster Area

8.27.18	Novel prognostic biomarkers identified by proximity extension assay are associated with major bleeding in patients with atrial fibrillation on oral anticoagulation: insights from the ARISTOTLE trial (Lars Wallentin et al./Poster)	Session: Poster Session 5: Atrial fibrillation – Stroke prevention 1	14:00-18:00	Poster Area
8.27.18	Cardiac troponin T concentrations are lower in women than men with atrial fibrillation but have similar prognostic value regardless of sex - insights from the ARISTOTLE trial (Helge Røsjø et al./Poster)	Session: Poster Session 5: Prevention – Cardiovascular risk assessment: biomarkers	14:00-18:00	Poster Area
8.27.18	Gastrointestinal bleeding is associated with gastrointestinal cancer in patients with atrial fibrillation treated with anticoagulants - A nationwide study (Peter Vibe Rasmussen et al./Poster)	Session: Atrial Fibrillation – Stroke Prevention	15:50-16:40	Poster Area
8.28.18	Faster heart rate is associated with significantly higher risk of death and hospitalization due to heart failure in patients with persistent or permanent atrial fibrillation: insights from ARISTOTLE (Dragos Vinereanu et al./Poster)	Session: Poster Session 6: Atrial fibrillation: prognosis outcomes	8:30-12:30	Poster Area
8.28.18	Comparison of effectiveness, safety, and healthcare costs of direct oral anticoagulants with warfarin in nonvalvular atrial fibrillation patients with heart failure (Alessandra Bassalobre Garcia et al./Poster)	Session: Poster Session 7: Atrial fibrillation – Epidemiology	14:00-18:00	Poster Area

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**Limitations of Real-World Data Analyses:** Real-world data have the potential to complement randomized controlled trial data by providing additional information about how a medicine performs in routine medical practice. Real-world data analyses have several limitations. For example, the source and type of data used may limit the generalizability of the results and of the endpoints. Observational real-world studies can only evaluate association and not causality. Due to these limitations, real-world data analyses are not used as stand-alone evidence to validate the efficacy and/or safety of a treatment. **It is important to note that, at this time, there are no head-to-head clinical trials comparing direct oral anticoagulants.**

**BMS-Pfizer Alliance Real-World Data (RWD) Program:** The Bristol-Myers Squibb-Pfizer Alliance global RWD analysis program, ACROPOLIS™ (Apixaban ExperienCe Through Real-WOrld POpuLatIon Studies) is designed to generate additional evidence from routine clinical practice settings to further inform healthcare decision makers, including healthcare providers and payers. The ACROPOLIS program includes retrospective, outcomes-based analyses of patients from 19 databases around the world, including anonymized medical records, medical and pharmacy health insurance claims data, and national health data systems. To date, the ACROPOLIS program includes a sample size of more than 970,000 lives spanning 11 countries.

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 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 multiple 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.
- The anticoagulant effect of apixaban can be expected to persist for at least 24 hours after the last dose (i.e., about two half-lives). An agent to reverse the anti-factor Xa activity of apixaban is available. Please visit [www.andexxa.com](http://www.andexxa.com) for more information on availability of a reversal agent.
- **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

- **Combined P-gp and Strong CYP3A4 Inhibitors:** Inhibitors of P-glycoprotein (P-gp) and cytochrome P450 3A4 (CYP3A4) 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 combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, or ritonavir). In patients already taking 2.5 mg twice daily, avoid coadministration of ELIQUIS with combined P-gp and strong CYP3A4 inhibitors.

### *Clarithromycin*

Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS.

- **Combined P-gp and Strong CYP3A4 Inducers:** Avoid concomitant use of ELIQUIS with combined P-gp and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban.
- **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](http://www.bms.com).**

### **About ARISTOTLE**

ARISTOTLE (Apixaban for **R**eduction In **S**troke 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, multinational 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](http://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](http://www.pfizer.com). In addition, to learn more, please visit us on [www.pfizer.com](http://www.pfizer.com) and follow us on Twitter at [@Pfizer](https://twitter.com/Pfizer) and [@PfizerNews](https://twitter.com/PfizerNews), [LinkedIn](https://www.linkedin.com/company/pfizer), [YouTube](https://www.youtube.com/pfizer) and like us on Facebook at [Facebook.com/Pfizer](https://www.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 the research, development and commercialization of pharmaceutical products. 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, 2017, 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.*

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**Pfizer Disclosure Notice** The information contained in this release is as of March 11, 2018. 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, 2017 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 U.S. Securities and Exchange Commission and available at [www.sec.gov](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com). Contact: Bristol-Myers Squibb Media: Rob Perry, 407-492-4616, [rob.perry@bms.com](mailto:rob.perry@bms.com) Investors: Timothy Power, 609-252-7509, [timothy.power@bms.com](mailto:timothy.power@bms.com) Pfizer Inc. Media: Neha Wadhwa, 212-733-2835, [neha.wadhwa@pfizer.com](mailto:neha.wadhwa@pfizer.com) Investors: Ryan Crowe, 212-733-8160, [ryan.crowe@pfizer.com](mailto:ryan.crowe@pfizer.com)