FINDINGS RELEASED FROM NAXOS, A FRENCH REAL-WORLD DATA ANALYSIS AND THE LARGEST REAL-WORLD DATA ANALYSIS ON ORAL ANTICOAGULANT EFFECTIVENESS AND SAFETY IN EUROPE AMONG PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION

- **Eliquis® (apixaban) was associated with a lower rate of major bleeding, stroke and systemic thromboembolic events compared to a vitamin K antagonist**
- **Results show Eliquis was associated with a lower rate of major bleeding and comparable rates of stroke and systemic thromboembolic events versus dabigatran or rivaroxaban**
- **This late-breaking presentation is one of 11 Bristol-Myers Squibb-Pfizer Alliance abstracts being presented at the European Society of Cardiology Congress 2019**

PRINCETON, N.J., and NEW YORK, N.Y., September 1, 2019 – The Bristol-Myers Squibb-Pfizer Alliance today announced findings from NAXOS (EvaluatioN of ApiXaban in strOke and Systemic embolism prevention in patients with nonvalvular atrial fibrillation in the real-life setting in France), the largest real-world data analysis on oral anticoagulant (OAC) effectiveness and safety in Europe among patients with non-valvular atrial fibrillation (NVAF). NAXOS is a retrospective cohort analysis including nearly all patients in France aged 18 years or older with NVAF newly initiating one of the OACs between 2014 and 2016 (n=321,501). In this analysis, Eliquis® (apixaban) use was associated with a lower rate of major bleeding compared to a vitamin K antagonist (VKA) (hazard ratio [HR]: 0.49, 95% confidence interval [CI]: 0.46-0.52), rivaroxaban (HR: 0.63, 95% CI: 0.58-0.67) and dabigatran (HR: 0.85, 95% CI: 0.76-0.95). These data were featured as a late-breaking oral presentation at the European Society of Cardiology (ESC) Congress 2019 in Paris, France (Abstract 1362). Anticoagulants, including Eliquis, increase the risk of bleeding and can cause serious, potentially fatal bleeding. Please see important safety information below for Eliquis, including BOXED WARNINGS.

In this analysis, Eliquis was also associated with lower rates of stroke and systemic thromboembolic events compared to VKA (HR: 0.67, 95% CI: 0.62-0.72) and rates similar to rivaroxaban (HR: 0.97, 95% CI: 0.89-1.05) or dabigatran (HR: 0.92, 95% CI: 0.81-1.06). Eliquis was associated with a lower rate of all-cause mortality compared to VKA (HR: 0.56, 95% CI: 0.54-0.58) and rivaroxaban (HR: 0.89, 95% CI: 0.85-0.93) and rates similar to dabigatran (HR: 0.94, 95% CI: 0.87-1.01). It is important to note that there are no head-to-head clinical trials comparing non-vitamin K antagonist OACs.

"The large-scale NAXOS retrospective observational analysis is significant because it included nearly the entire French population with NVAF and is the first nationwide analysis that has evaluated the effectiveness and safety of all available OACs in France," said **Professor Philippe Gabriel Steg, M.D., FESC, FACC, Head of Cardiology Department at Hôpital Bichat, Assistance Publique-Hôpitaux de Paris and Professor at Université de Paris.** *"Being able to analyze data from routine clinical practice from a large patient population may help characterize the effectiveness and safety of available anticoagulants."*

Real-world data have the potential to complement randomized controlled clinical trial data by providing additional information about how a medicine performs in routine medical practice. Real-world data analyses also have several limitations. For example, the source and type of data used may limit the generalizability of the results and endpoints. Observational real-world studies can only evaluate association and not causality, and despite the use of methods to address measured confounding, residual confounding may still be present. Due to its limitations, real-world data analyses are not used as stand-alone evidence to validate the efficacy and/or safety of a treatment.

In this analysis, although propensity score adjustment was used to control for multiple confounders, there is still potential for residual bias. Claims for a filled prescription do not indicate that the medication was consumed or taken as prescribed. Also, over-the-counter medications, such as aspirin, and prescription medications provided as samples are not captured in the claims data.

The NAXOS analysis included nearly all patients in France aged 18 years or older with NVAF newly initiating one of the OACs between 2014 and 2016. Patients were identified in the French national health insurance database, SNIIRAM, which covers almost the entire population living in France. The primary objectives were to describe the real-world use of Eliquis and the other OACs available in France, and to evaluate the comparative rates of major bleeding (safety), stroke and systemic thromboembolic events (effectiveness), and all-cause mortality in patients with NVAF initiating OAC treatment. Three sensitivity analyses were performed using adjustment on confounding factors, propensity score matching and high-dimensional propensity score matching.

"Results from the NAXOS real-world data analysis of NVAF patients in France add to the growing body of real-world evidence for Eliquis, which now includes a sample size of over two million lives globally," said **Dr. Rory O'Connor, Chief Medical Officer, Pfizer Internal Medicine.** *"We are committed to gaining additional insights about how a treatment performs in the real world to help practicing physicians around the world make informed decisions."*

The prevalence of atrial fibrillation in France was estimated to be between 600,000 and one million people in 2011, according to the most recent available data.

"As the real-world evidence landscape continues to advance, we are able to provide additional insights from a growing amount of patient data from around the world," said **Mary Beth Harler, Head of Innovative Medicines Development, Bristol-Myers Squibb**. *"Healthcare practices and patient demographics can differ across geographies, and real-world data from the French NAXOS analysis can help provide healthcare practitioners in the region with relatable insights for their patients with NVAF."*

At this year's ESC Congress, the BMS-Pfizer Alliance presented a total of 11 abstracts, including the NAXOS oral presentation and NAXOS moderated ePoster, presented on September 1, 2019. For a searchable list of abstracts presented during ESC Congress 2019 visit: http://bit.ly/ESCCongress19.

BMS-Pfizer Alliance Real-Word Data Program: NAXOS is part of the Bristol-Myers Squibb-Pfizer Alliance global real-world data analysis program, ACROPOLIS™ (Apixaban ExperienCe Through Real-WOrld POpuLatIon Studies), designed to generate additional evidence from routine clinical practice settings to further inform healthcare decision makers, including healthcare providers and payers. These analyses 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. The ACROPOLIS program currently includes analyses of patients from more than 20 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 two million lives spanning more than 10 countries.

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. The approval of Eliquis for stroke risk reduction in patients with NVAF is based on data from the Phase 3 ARISTOTLE and AVERROES studies of Eliquis in patients with NVAF.

U.S. FDA-Approved Indications for Eliquis: Eliquis is a prescription medicine indicated in the U.S. to reduce the risk of stroke and systemic embolism in patients with 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.

ABOUT PFIZER INC.: BREAKTHROUGHS THAT CHANGE PATIENTS' LIVES

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, including innovative medicines and vaccines. 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 160 years, we have worked to make a difference for all who rely on us.

i Value of a national administrative database to guide public decisions: From the système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the système national des données de santé (SNDS) in France. Available from: https://www.researchgate.net/publication/318736432_Value_of_a_national_administrative_database_to_guide_public_decisions_From_the_systeme_national_d%27information_interregimes_de_l%27Assurance_Maladie_SNIIRAM_to_the_systeme_national_des_donnees_de_sante_S [accessed Jun 07 2019]

ii Epidemiology of atrial fibrillation in France: Extrapolation of international epidemiological data to France and analysis of French hospitalization data. (2011, March 02). Retrieved from https://www.sciencedirect.com/science/article/pii/S1875213611000209