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News Release

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Bayer's NAVIGATE ESUS study halted early as it indicated comparable efficacy between treatment arms

- Phase III NAVIGATE ESUS study evaluated rivaroxaban vs aspirin in patients with embolic stroke of undetermined source (ESUS)
- The study at interim indicates no efficacy improvement over low dose aspirin and very little chance of showing overall benefit if the study were completed
- The positive benefit risk profile of rivaroxaban remains unchanged in all licensed indications

Berlin, October 5, 2017 – Bayer AG and its development partner Janssen Research & Development, LLC today announced that the Phase III NAVIGATE ESUS study evaluating the efficacy and safety of rivaroxaban (Xarelto[®]) for the secondary prevention of stroke and systemic embolism in patients with a recent embolic stroke of undetermined source (ESUS) has been stopped early. Based on the recommendation by the Independent Data Monitoring Committee (IDMC) following a planned interim analysis, the trial was halted early as it showed comparable efficacy between the rivaroxaban and aspirin arms and very little chance of showing overall benefit if the study were completed. While bleeding rates were low overall, an increase in bleeding was observed in the rivaroxaban arm compared to the low dose aspirin arm. The decision to halt the trial was taken jointly by the Academic Leadership of the trial and the sponsor Bayer.

ESUS refers to patients with embolic stroke documented by neuroimaging for which the cause remains unidentified despite thorough investigations attempting to rule out established cardiac and vascular sources. It does not include patients with atrial fibrillation or established atherosclerotic disease and therefore the patient population in NAVIGATE ESUS differs from the currently approved indications for rivaroxaban. Despite recommended treatments, the stroke recurrence risk for patients with ESUS remains substantial.

“Patients with ESUS currently have limited treatment options and the role of anticoagulants in this area remains uncertain. We will now analyze the data from NAVIGATE ESUS to better understand this outcome and its implications,” said Dr Joerg Moeller, Member of the Executive Committee of Bayer AG's Pharmaceutical Division and Head of Development. “Patients will be contacted by their physician to switch to standard of care, aspirin. Patients should not stop trial medication without consultation of their physicians. We are committed to continuing the extensive investigation of rivaroxaban for patients at risk of deadly blood clots.”

The Phase III NAVIGATE ESUS¹ study has enrolled 7,214 patients from 459 sites across 31 countries worldwide. In the study, patients were randomized to receive either rivaroxaban 15 mg once daily or aspirin 100 mg once daily alone. The primary efficacy endpoint was a composite of stroke (ischemic, hemorrhagic and undefined stroke, transient ischemic attack with positive neuroimaging) and systemic embolism. The primary safety endpoint was major bleeding according to the criteria of the International Society on Thrombosis and Haemostasis (ISTH). A complete data analysis is expected to be presented at an upcoming medical meeting in 2018.

About Xarelto[®] (Rivaroxaban)

Rivaroxaban is the most broadly indicated non-vitamin K antagonist oral anticoagulant (NOAC) and is marketed under the brand name Xarelto[®]. Xarelto is approved for seven indications, protecting patients across more venous and arterial thromboembolic (VAT) conditions than any other NOAC:

- The prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF) and one or more risk factors
- The treatment of pulmonary embolism (PE) in adults
- The treatment of deep vein thrombosis (DVT) in adults
- The prevention of recurrent PE and DVT in adults
- The prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip replacement surgery

- The prevention of VTE in adult patients undergoing elective knee replacement surgery
- The prevention of atherothrombotic events (cardiovascular death, myocardial infarction or stroke) after an Acute Coronary Syndrome in adult patients with elevated cardiac biomarkers and no prior stroke or transient ischaemic attack (TIA) when co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine

Whilst licences may differ from country to country, across all indications Xarelto is approved in more than 130 countries.

Rivaroxaban was discovered by Bayer, and is being jointly developed with Janssen Research & Development, LLC. Xarelto is marketed outside the U.S. by Bayer and in the U.S. by Janssen Pharmaceuticals, Inc. (Janssen Research & Development, LLC and Janssen Pharmaceuticals, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson).

Anticoagulant medicines are potent therapies used to prevent or treat serious illnesses and potentially life-threatening conditions. Before initiating therapy with anticoagulant medicines, physicians should carefully assess the benefit and risk for the individual patient.

Responsible use of Xarelto is a very high priority for Bayer, and the company has developed a Prescribers Guide for physicians and a Xarelto Patient Card for patients to support best practice.

To learn more about thrombosis, please visit www.thrombosisadviser.com

To learn more about Xarelto, please visit www.xarelto.com

Bayer: Science For A Better Life

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citizen. In fiscal 2016, the Group employed around 115,200 people and had sales of EUR 46.8 billion. Capital expenditures amounted to EUR 2.6 billion, R&D expenses to EUR 4.7 billion. These figures include those for the high-tech polymers business, which was floated on the stock market as an independent company named Covestro on October 6, 2015. For more information, go to www.bayer.com

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¹ New Approach rivaroxaban Inhibition of factor Xa in a Global trial vs ASA to prevenT Embolism in Embolic Stroke of Undetermined Source