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Daiichi-Sankyo

Press Release

Daiichi Sankyo Initiates ELIMINATE-AF Study Investigating Once-Daily Lixiana® (edoxaban) in Patients Undergoing Catheter Ablation of Non-valvular Atrial Fibrillation

- *Study adds to the growing Edoxaban Clinical Research Program (ECRP) evaluating its use in a broad range of cardiovascular conditions, patient types and clinical settings*

Tokyo, Japan, (March 31, 2017) – Daiichi Sankyo Company, Limited (hereafter, "Daiichi Sankyo") today announced that the first patient has been enrolled into the ELIMINATE-AF study. The multinational, randomized phase 3b study will explore the safety and efficacy of the company's oral, once-daily direct factor Xa-inhibitor edoxaban (known by the brand name LIXIANA® outside the US and SAVAYSA® in the US) against a vitamin K antagonist in patients with atrial fibrillation (AF) undergoing catheter ablation. The study will investigate the incidence of the composite of all-cause death, stroke and major bleeding (International Society on Thrombosis and Hemostasis [ISTH] definition).[1] Approximately 560 patients will be enrolled in ELIMINATE-AF from 75 clinical sites across Europe, Canada and Asia.[1]

"Catheter ablation as a method of treating AF is more frequently performed in clinical practice due to its positive effect on AF-related symptoms and quality of life; however, it is associated with a significant thromboembolic risk during and shortly after the procedure," said Stefan Hohnloser, MD, Professor of Medicine and Cardiology, Head, Department of Electrophysiology, Johann Wolfgang Goethe University in Frankfurt, Germany, and principal study investigator. "ELIMINATE-AF will provide insights into the use of edoxaban for uninterrupted anticoagulation in patients undergoing catheter ablation, applying state-of-the-art treatment in accordance with the recent treatment guidelines. In this study, edoxaban will be used with the approved dosage regimen for stroke prevention in atrial fibrillation"

"Following the positive results of the use of edoxaban in the ENSURE-AF cardioversion study, we now look forward to evaluating the use of edoxaban in patients undergoing cardiac ablation with ELIMINATE-AF," said Hans J. Lanz, MD, Executive Director, Global Medical Affairs, Daiichi Sankyo. "Importantly, the study will add to the growing body of evidence in the Edoxaban Clinical Research Program, and help to broaden clinicians' understanding of the concept of uninterrupted anticoagulation for catheter ablation."

About ELIMINATE-AF

Eva**L**uat**I**on of Edoxaban co**M**pared with VKA **IN** subjects undergoing c**AT**h**E**ter ablation of non-valvular **A**trial **F**ibrillation (ELIMINATE-AF) is a prospective, randomized, open-label, blinded endpoint evaluation, parallel-group phase 3b study to evaluate the efficacy and safety of once-daily edoxaban against a vitamin K antagonist in AF patients undergoing catheter ablation of AF. The primary objective is to descriptively compare the incidence of the composite of all-cause death, stroke (ischemic, hemorrhagic, or undetermined) and major bleeding (ISTH definition) in the edoxaban group against the vitamin K antagonist group in the period from the end of the catheter ablation procedure to Day 90/end-of-treatment (EOT). The primary safety objective is to descriptively compare the incidence of major bleeding (ISTH definition) in the edoxaban group against the VKA group in the period from date of first intake of study medication to Day 90/EOT. Approximately 560 patients will be enrolled in ELIMINATE-AF from 75 clinical sites across Europe, Canada and Asia. Patients will be randomized to receive edoxaban or VKA for 21 days pre- and 90 days post-ablation period.[1]

Before catheter ablation, all patients will undergo transesophageal echocardiography (or alternatively intracardiac echocardiography) to exclude atrial thrombi and thus minimize the risk of stroke. The study will use the approved edoxaban dosage regimen for stroke prevention in AF patients in each country. In addition, at pre-selected centers, Diffusion Weighted Magnetic Resonance Imaging (DW-MRI) will be used to detect silent cerebral lesions post ablation procedure.

For more information, please visit: https://clinicaltrials.gov/ct2/show/NCT02942576

About Atrial Fibrillation

AF is a condition where the heart beats irregularly and rapidly. When this happens, blood can pool and thicken in the chambers of the heart causing an increased risk of blood clots. These blood clots can break off and travel through the blood stream to the brain (or sometimes to another part of the body), where they have the potential to cause a stroke.[2]

AF is the most common type of heart rhythm disorder, and is associated with substantial morbidity and mortality.[3] More than six million Europeans are diagnosed with AF, and this figure is expected to at least double over the next 50 years.[4,5] Compared to those without AF, people with the arrhythmia have a 3-5 times higher risk of stroke.[6] One in five of all strokes are as a result of AF.[4]

About Edoxaban

Edoxaban is an oral, once-daily, direct factor Xa (pronounced “Ten A”) inhibitor. Factor Xa is one of the key components responsible for blood clotting, so inhibiting this makes the blood thin and less prone to clotting. Edoxaban is currently marketed in Japan, the U.S., South Korea, Hong Kong, Taiwan, Thailand, Switzerland, the U.K., Germany, Ireland, the Netherlands, Italy, Spain, Belgium, Austria, Portugal, and other European countries.

About Edoxaban Clinical Research Program (ECRP)

Daiichi Sankyo is committed to expanding scientific knowledge about edoxaban, as demonstrated through our research programs evaluating its use in a broad range of cardiovascular conditions, patient types and clinical settings in atrial fibrillation (AF) and venous thromboembolism (VTE). The edoxaban clinical research program includes multiple RCTs (randomized, controlled trials), registries and non-interventional studies, with the goal of generating new clinical and real-world-data regarding its use in AF and VTE populations. Daiichi Sankyo expects that more than 100,000 patients will participate in the edoxaban clinical research program, including completed, ongoing and future research.

The RCTs include:

- ENSURE-AF (EdoxabaN vs. warfarin in subjectS UndeRgoing cardiovErsion of Atrial Fibrillation), in AF patients undergoing electrical cardioversion
- ENTRUST-AF PCI (EdoxabaN TReatment versUS VKA in paTients with AF undergoing PCI), in AF patients undergoing percutaneous coronary intervention
- Hokusai-VTE Cancer (Edoxaban in Venous Thromboembolism Associated with Cancer), in patients with cancer and an acute VTE event
- ELDERCARE-AF (Edoxaban Low-Dose for EldeR CARE AF patients), in elderly AF patients in Japan
- ELIMINATE-AF (EvaLuatIon of edoxaban coMpared with VKA IN subjects undergoing cAThEter ablation of non-valvular Atrial Fibrillation)
- ENVISAGE-TAVI AF (EdoxabaN Versus standard of care and theIr effectS on clinical outcomes in pAtients havinG undergonE Transcatheter Aortic Valve Implantation (TAVI) – Atrial Fibrillation)

In addition, global and regional registry studies will provide important real-world data about the use of edoxaban and other oral anticoagulants in everyday practice, and include:

- ETNA-AF (Edoxaban Treatment in routiNe clinical prActice in patients with non valvular Atrial Fibrillation)
- ETNA-VTE (Edoxaban Treatment in routiNe clinical prActice in patients with Venous ThromboEmbolism)
- EMIT-AF/VTE (Edoxaban Management In diagnostic and Therapeutic procedures-AF/VTE);
- Prolongation PREFER in AF (PREvention oF thromboembolic events – European Registry) in patients with AF
- ANAFIE (All Nippon AF In Elderly) Registry in Japan
- Cancer-VTE Registry in Japan

We are committed to adding to the scientific body of knowledge around edoxaban in a variety of AF and VTE patients, including those who are vulnerable.

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address diversified, unmet medical needs of patients in both mature and emerging markets. With over 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 16,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to a strong portfolio of medicines for hypertension and thrombotic disorders, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo research and development is primarily focused on bringing forth novel therapies in oncology, including immuno-oncology, with additional focus on new horizon areas, such as pain management, neurodegenerative diseases, heart and kidney diseases, and other rare diseases. For more information, please visit: www.daiichisankyo.com.

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Forward-looking statements

This press release contains forward-looking statements and information about future developments in the sector, and the legal and business conditions of DAIICHI SANKYO Co., Ltd. Such forward-looking statements are uncertain and are subject at all times to the risks of change, particularly to the usual risks

faced by a global pharmaceutical company, including the impact of the prices for products and raw materials, medication safety, changes in exchange rates, government regulations, employee relations, taxes, political instability and terrorism as well as the results of independent demands and governmental inquiries that affect the affairs of the company. All forward-looking statements contained in this release hold true as of the date of publication. They do not represent any guarantee of future performance. Actual events and developments could differ materially from the forward-looking statements that are explicitly expressed or implied in these statements. DAIICHI SANKYO Co., Ltd. assume no responsibility for the updating of such forward-looking statements about future developments of the sector, legal and business conditions and the company.

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