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Press Release

New LIXIANA® sub-analysis from the ENGAGE AF-TIMI 48 trial presented at the American Heart Association Annual Scientific Sessions 2017

- *A sub-analysis of the ENGAGE AF-TIMI 48 trial found that edoxaban had even greater reductions in ischaemic events compared to warfarin in patients with atrial fibrillation (AF) and coronary artery disease (CAD)*

Tokyo, Japan (November 15, 2017) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo), today announced results of a sub-analysis from its global phase 3 ENGAGE AF-TIMI 48 trial that evaluated the safety and efficacy profile of edoxaban (the brand name LIXIANA®) in patients with AF. It included a post-hoc analysis from the ENGAGE AF-TIMI 48 trial, providing insights on edoxaban in AF patients with established CAD, and found those on an edoxaban regimen (60/30 mg) versus warfarin had greater reductions in ischaemic events, compared to those without CAD. The data was presented at the American Heart Association (AHA) Scientific Sessions on 11 – 15 November in Anaheim, California.

In the sub-analysis, findings showed that among AF patients with known CAD, those treated with edoxaban compared to warfarin, had greater reductions in stroke/systemic embolic events (SEE) (1.4 versus 2.1%) and myocardial infarction (MI) (1.4 versus 2.0%), compared to patients without CAD [stroke/SEE in edoxaban vs warfarin (1.6 versus 1.7%); MI in edoxaban vs warfarin (0.5 versus 0.4%)].[2] Major bleeding rates in patients who received edoxaban were significantly lower than in patients who received warfarin, regardless of CAD status [CAD patients on edoxaban versus warfarin (3.6 versus 4.4%); patients without CAD on edoxaban versus warfarin (2.5 versus 3.2%)].[2]

“Since patients with atrial fibrillation and concomitant coronary artery disease are at higher risk of myocardial infarction and death, these results may have important clinical implications for physicians who treat these common conditions”, said study author Thomas A Zelniker, TIMI Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA.

The ENGAGE AF-TIMI 48 trial was designed to study the safety and efficacy of edoxaban compared to warfarin in patients with AF (n=21,105) and moderate to high risk for stroke ($CHADS_2 \geq 2$) or SEE.[3]

"These data from the ENGAGE AF-TIMI 48 trial will add to the growing body of knowledge in the Edoxaban Clinical Research Programme, which provides key insights into the potential effects of edoxaban in AF patients, in this case for those with coronary artery disease," said Hans J. Lanz, MD, Vice President, Global Medical Affairs, Daiichi Sankyo.

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About the ENGAGE AF-TIMI 48 Study

The ENGAGE AF-TIMI 48 global phase 3 study investigated once-daily edoxaban in comparison to warfarin in 21,105 patients with NVAF. This represented the largest and longest trial with a NOAC in patients with AF performed to date, with a median follow-up of 2.8 years. Edoxaban demonstrated non-inferiority for stroke or systemic embolism (SE) in comparison to warfarin. Edoxaban was also found to be superior for the principal safety endpoint of major bleeding in comparison to warfarin.[3]

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.[4]

AF is the most common type of heart rhythm disorder, and is associated with substantial morbidity and mortality.[5] Compared to those without AF, people with the arrhythmia have a 3-5 times higher risk of stroke.[7] One in five of all strokes are as a result of AF.[8]

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 by Daiichi Sankyo and its partners in more than 20 countries around the world.

About Edoxaban Clinical Research Programme (ECRP)

Daiichi Sankyo is committed to expanding scientific knowledge about edoxaban, as demonstrated through our research programmes evaluating its use in a broad range of cardiovascular conditions, patient types and clinical settings in AF and VTE. The edoxaban clinical research programme includes multiple RCTs (randomised, 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 programme, 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 15,000 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.

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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