

Press Release

Daiichi Sankyo's Once-Daily LIXIANA® (edoxaban) Approved in the EU for Stroke Prevention in Nonvalvular Atrial Fibrillation and for the Treatment and Prevention of Recurrent DVT and PE

- *EU approval paves the way for LIXIANA® (edoxaban) to be made available across all European member states*
- *Marketing authorisation is based on data from the ENGAGE AF-TIMI 48 and Hokusai-VTE studies, the largest single comparative global trials of a novel oral anticoagulant in patients with nonvalvular atrial fibrillation or venous thromboembolism, involving 21,105 and 8,292 patients, respectively*
- *LIXIANA®, a factor Xa-inhibitor, is a once-daily oral anticoagulant that combines proven efficacy and a significantly better bleeding profile* than well-managed warfarin*

Tokyo, Japan (June 25, 2015) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced that the European Commission (EC) has granted Marketing Authorisation for LIXIANA® (edoxaban), an oral, once-daily selective factor Xa-inhibitor, for the prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation (NVAF) with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack (TIA) as well as for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

“AF-related stroke as well as DVT and PE create a significant societal and economic health burden. We welcome the European Commission’s approval of LIXIANA, which means physicians and patients may benefit from a new treatment option to effectively manage these debilitating and life-threatening conditions,” said Jan van Ruymbeke, MD, CEO, Daiichi Sankyo Europe GmbH. “Daiichi Sankyo is committed to bringing innovative medicines to patients who need them. Once-daily

*Major bleeding in NVAF, clinically relevant non-major bleeding in VTE (composite of major bleeding and clinically relevant non-major bleeding)

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LIXIANA offers the unique combination of an easy-to-use oral anticoagulant with proven efficacy across a broad range of patients and a better bleeding profile compared to well-managed warfarin.”

Atrial fibrillation (AF), a heart rhythm disorder in which the heartbeat is rapid and irregular, affects over six million Europeans.¹ People with AF are at a five-fold increased risk of stroke compared to the general population,¹ with an estimated financial burden of over €38 billion a year.² VTE, a condition where a blood clot forms in a vein, also represents a major cause of morbidity and mortality, resulting in over 500,000 deaths in the EU each year.³

The EC approval is based on two phase 3 clinical trials, ENGAGE AF-TIMI 48 and Hokusai-VTE, which compared treatment with once-daily LIXIANA® to warfarin, a current standard of care for stroke prevention in patients with AF or for the treatment and prevention of VTE. These studies represent the largest single comparative trials of a novel oral anticoagulant in these patient populations, involving 21,105 and 8,292 patients, respectively.^{4,5}

In the ENGAGE AF-TIMI 48 study, once-daily LIXIANA® showed comparable efficacy (stroke or SEs) in comparison to warfarin (1.18% vs. 1.50% per year, LIXIANA® 60 mg vs. warfarin respectively; hazard ratio [HR], 0.79; 97.5% confidence interval [CI], 0.63 to 0.99, p<0.001) and superior safety, significantly reducing major bleeding (2.75% vs. 3.43% per year, LIXIANA® 60 mg vs. warfarin respectively; HR, 0.80; 95% CI, 0.71 to 0.91, p<0.001), in a broad range of patients with NVAf.⁴

The Hokusai-VTE study demonstrated that LIXIANA® effectively reduces symptomatic recurrent VTE, including DVT and fatal and non-fatal PE risk across a broad range of patients (3.2% vs. 3.5% of patients, LIXIANA® 60 mg vs. warfarin respectively; HR, 0.89; 95% CI, 0.70 to 1.13, p<0.001). LIXIANA® also showed a significant 19% risk reduction of clinically relevant bleeding in patients with VTE compared to warfarin (8.5% vs. 10.3% of patients, respectively; HR, 0.81; 95% CI, 0.71 to 0.94, p=0.004).⁵

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About LIXIANA® (edoxaban)

Once-daily LIXIANA® was developed solely by Daiichi Sankyo. It was launched in Switzerland in May 2015 for the prevention of stroke and SE in adult patients with NVAf, and for the treatment of adult patients with VTE, including DVT and PE, following previous treatment with fractionated or unfractionated heparin for five days, as well as for the prevention of recurrent VTE.⁶ In addition, it is currently marketed in Japan and the United States.^{7,8,9} In other countries, regulatory review is ongoing.

About the ENGAGE AF-TIMI 48 Study

ENGAGE AF-TIMI 48 (Effective aNticoagulation with factor xA next GEneration in Atrial Fibrillation) was a three-arm, randomized, double-blind, double-dummy, global phase 3 clinical trial comparing once-daily edoxaban with warfarin in 21,105 patients with NVAf at moderate-to-high risk of thromboembolic events at 1,393 centers in 46 countries. ENGAGE AF-TIMI 48 compared two edoxaban treatment strategies, a higher dose arm (60 mg or 30 mg dose reduced) once-daily and a lower dose arm (30 mg or 15 mg dose reduced) once-daily, with warfarin in patients with NVAf for a median of 2.8 years. Patients were dose reduced for creatinine clearance (CrCL) 30 to 50 mL/min, body weight of 60 kg or less or certain p-glycoprotein inhibitor use. ENGAGE AF-TIMI 48 represents the largest and longest single comparative global trial with a novel anticoagulant in patients with NVAf performed to date.⁴ The full results were presented at the AHA Scientific Sessions 2013 in Dallas and published in the New England Journal of Medicine.

About the Hokusai-VTE Study

Hokusai-VTE was a global, event-driven, randomized, double-blind, double-dummy, parallel-group phase 3 clinical study involving 8,292 patients in 439 clinical sites across 37 countries to evaluate once-daily edoxaban with warfarin in patients with either acute symptomatic DVT, PE or both. The Hokusai-VTE study was designed to reflect clinical practice using a flexible treatment duration of 3-12 months in a broad spectrum of VTE patients, including initial use of parenteral anticoagulant (heparin) for at least 5 days, the proven global standard of care. Patients were randomized to receive initial open-label enoxaparin or unfractionated heparin therapy followed by edoxaban 60 mg once-daily (dose reduced to 30 mg for CrCL 30 to 50 mL/min, body weight of 60 kg or less, or certain p-glycoprotein inhibitor use) or the comparator, warfarin. In the comparator arm, patients received initial heparin therapy concurrently with warfarin, titrated to a target INR of 2.0 to 3.0, followed by warfarin alone.

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The treatment duration was from 3 months and up to a maximum of one year. The duration of study treatment was determined by the investigator based on the patient's clinical features.⁵ The full results were presented at the ESC Congress 2013 in Amsterdam and published in the New England Journal of Medicine.

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 17,000 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 its strong portfolio of medicines for hypertension, dyslipidemia, bacterial infections, and thrombotic disorders, the Group's research and development is focused on bringing forth novel therapies in cardiovascular-metabolic diseases, pain management, and oncology, including biologics. 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

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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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