# Edoxaban Significantly Reduces Risk of Venous Thromboembolism by Half Compared to Enoxaparin in Japanese and Taiwanese Patients Following Knee or Hip Arthroplasty Surgery

***Pooled results of the STARS E-III and STARS J-V studies presented at the 2011 American Society of Hematology (ASH) Annual Meeting***

**TOKYO and SAN DIEGO** (December 12, 2011) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced the results of a pooled analysis showing that edoxaban, a direct oral once-daily factor Xa inhibitor, significantly reduced the risk of developing venous thromboembolism (VTE) following total knee or hip arthroplasty, when compared to enoxaparin. Patients receiving edoxaban had a lower incidence of a composite of deep vein thrombosis (DVT) and pulmonary embolism (PE) than those treated with enoxaparin (5.1 percent vs. 10.7 percent, P<0.001, Relative Risk Reduction [RRR] 52.7 percent), an effect that was shown without a statistically significant difference in bleeding between the groups.

The analysis drew data from two randomized, double-blind, double-dummy, Phase III studies (STARS E-III[i] and STARS J-V[ii]) of 1,326 Japanese and Taiwanese patients who underwent total knee arthroplasty (TKA) or total hip arthroplasty (THA). Results were presented in an oral session at the 53rd Annual Meeting of the American Society of Hematology in San Diego, USA.[iii]

"Total hip and knee arthroplasty surgeries place patients at a higher risk of DVT, which can lead to thromboembolic disease such as PE," said Dr. Takeshi Fuji, Head of Orthopedic Surgery, Osaka Koseinenkin Hospital, Osaka, Japan. "As the number of these surgeries increases, and the incidence of VTE is expected to double by the year 2050, it will become increasingly important for physicians to have a number of treatment options to prevent DVT and PE following these surgeries."[iv]

The incidence of major and Clinically Relevant Non-Major (CRNM) bleeding events in the edoxaban and enoxaparin groups was 4.6 percent vs. 3.7 percent, respectively (P=0.427). A further subgroup analysis of major and CRNM bleeding indicated no significant difference between edoxaban and enoxaparin in any of the patient subgroups evaluated, based on age, weight, or creatinine clearance.

Patients enrolled in the STARS E-III (Japanese and Taiwanese patients) and STARS J-V (Japanese patients) studies were randomized to receive either oral edoxaban 30 mg once daily or subcutaneous enoxaparin 20 mg (2000 IU) twice daily for 11 to 14 days, in line with standard clinical practice in Japan.[i, ii]

“We are pleased to see positive outcomes with edoxaban in this patient population,” said Dr. Kazunori Hirokawa, Global Head of R&D Unit, Daiichi Sankyo Co., Ltd. “These results further support the safety and efficacy of edoxaban in the prevention of DVT and PE following major orthopedic surgery. Daiichi Sankyo remains committed to developing edoxaban in our global clinical trials program.”

**About Edoxaban**

Edoxaban is a once-daily oral anticoagulant that directly inhibits Factor Xa, an important factor in the coagulation process. Edoxaban is currently available only in Japan, licensed for the prevention of venous thromboembolism (VTE) in patients undergoing total knee arthroplasty, total hip arthroplasty and hip fracture surgery. Daiichi Sankyo continues to develop edoxaban at a global level as a potential new treatment for stroke prevention in atrial fibrillation, and the treatment and prevention of recurrent VTE. Notably, Daiichi Sankyo has more than 25 years experience conducting research in the area of Factor Xa inhibition and was the first company to study these compounds in humans.

**About the Pooled STARS Analysis**

The analysis drew data from two Phase III comparative studies, STARS E-III and STARS J-V.

- The STARS E-III[1] study was a double-blind, enoxaparin-controlled, randomized study comparing edoxaban 30 mg once daily and enoxaparin 20 mg (2,000 IU) in the prevention of VTE in a total of 716 Japanese and Taiwanese patients undergoing TKA.[i]

- The STARS J-V[2] study was a double-blind, enoxaparin-controlled, randomized study comparing edoxaban 30 mg once daily and enoxaparin 20 mg (2,000 IU) in the prevention of VTE in 610 Japanese patients undergoing THA.[ii]

Both studies supported the March 2010 edoxaban New Drug Application (NDA) in Japan seeking approval for the prevention of VTE after major orthopedic surgery. In the studies, edoxaban was initiated six to 24 hours after surgery; enoxaparin was initiated 24 to 36 hours after surgery, the standard of care in Japan. The primary efficacy outcome in both studies was the composite of symptomatic and asymptomatic DVT and PE. The principal safety outcome was incidence of major and clinically relevant non-major bleeding.

**About Venous Thromboembolism**

VTE is the term for the generation of a blood clot within a vein, or the subsequent breaking off of that clot into a pulmonary (lung) artery. Deep vein thrombosis (DVT) and pulmonary embolism (PE) are the two sub-types of VTE. DVT is a blood clot anywhere in the deep veins of the legs, pelvis or arms. PE is a clot that detaches from the vein and travels to the lungs, lodging in the pulmonary arteries causing a potentially fatal condition. PE is often accompanied by DVT and a DVT can develop into a PE suddenly. Patients with diagnosed VTE are treated for three to six months (and sometimes even longer) based on their individual risk profile to prevent a second (recurrent) DVT or PE. VTE is the cause of significant mortality; 30 percent of people with VTE die within one month of diagnosis and about 25 percent of those with PE experience sudden death. Additionally, about 30 percent of those affected will experience a recurrence of DVT/PE within 10 years of the initial DVT/PE diagnosis.[vii]

**About Daiichi Sankyo**

The Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address the diversified, unmet medical needs of patients in both mature and emerging markets. While maintaining its portfolio of marketed pharmaceuticals for hypertension, hyperlipidemia, and bacterial infections, the Group is engaged in the development of treatments for thrombotic disorders and focused on the discovery of novel oncology and cardiovascular-metabolic therapies. Furthermore, the Daiichi Sankyo Group has created a "Hybrid Business Model," which will respond to

market and customer diversity and optimize growth opportunities across the value chain.

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, DAIICHI SANKYO, Inc., and DAIICHI SANKYO EUROPE GmbH. 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, DAIICHI SANKYO, Inc., and DAIICHI SANKYO EUROPE GmbH 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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[i] T. Fuji et al., Edoxaban versus enoxaparin for thromboprophylaxis after total knee replacement: The STARS E-III trial 21st International Congress of Thrombosis, July 6 -9 2010, Milano, Italy.

[ii] T. Fuji et al., Efficacy and safety of edoxaban versus enoxaparin for the prevention of venous thromboembolism following total hip arthroplasty: STARS J-V trial, December 4-7, 2010, Orlando, Florida.

[iii] T. Fuji et al., Edoxaban versus enoxaparin for the prevention of venous thromboembolism: pooled analysis of venous thromboembolism and bleeding from STARS E-III and STARS J-V: The 53rd American Society of Hematology Annual Meeting and Exposition, December 10-13, 2011.

[iv] *Journal of Thrombosis and Haemostasis* 2007; Volume 5, Supplement 2: abstract number OC-WE-018. http://www.blackwellpublishing.com/isth2009/abstract.asp?id=76605. Accessed February 4, 2011.

[vii] Beckman MG et al. Public health research activities in venous thromboembolism. *Arterioscler Thromb Vasc Biol*. 2008; 394-5.