Data from Phase 3b ENSURE-AF Study Investigating Once-Daily SAVAYSA® (edoxaban) in Patients with Atrial Fibrillation Undergoing Cardioversion Among 13 Daiichi Sankyo Clinical Presentations at ESC Congress 2016

- *ENSURE-AF results to be featured during a late-breaking clinical trial session*
- *Five abstracts highlighting analyses from the global phase 3 ENGAGE AF-TIMI 48 study to be presented*
- *Seven abstracts to reveal new findings from the PREFER in AF and VTE European patient registries*

Parsippany, NJ (August 24, 2016) – Daiichi Sankyo, Inc. (hereafter, Daiichi Sankyo) today announced the presentation of 13 abstracts at the ESC Congress 2016, taking place from August 27-31 in Rome, Italy. The first results from ENSURE-AF, the largest prospective randomized clinical trial to date evaluating a non-vitamin K antagonist oral anticoagulant (NOAC) compared to a current standard of care in patients with non-valvular atrial fibrillation (NVAF) undergoing electrical cardioversion, which included nearly 2,200 patients from 19 countries, will be featured in a late-breaking clinical trial presentation. In addition, five analyses from the global phase 3 ENGAGE AF-TIMI 48 study of edoxaban (known by the brand name LIXIANA® outside the US and SAVAYSA® in the US) will be presented, including clinical outcomes associated with dose interruption in patients with NVAF compared to warfarin, relationship between body mass index and clinical outcomes, and a novel risk prediction score for net clinical outcome assessment.

Furthermore, six analyses from the PREFER in atrial fibrillation (AF) registry and one analysis from the PREFER in venous thromboembolism (VTE) registry will be presented, with new insights into the use of NOAC therapy, including prescribing patterns and trends in acute and long-term management of patients with AF and VTE.

Details of the presentations are included below:

Presentation Title	Presenter	Session Details
Late-breaking Oral Presentation		
Edoxaban for Cardioversion of Atrial Fibrillation: The Edoxaban Versus Warfarin in Subjects Undergoing Cardioversion of Atrial Fibrillation (ENSURE-AF) Study	Andreas Goette, MD, St. Vincenz-Hospital, Paderborn, Germany	Tuesday, August 30, 2:00-2:15 PM CET Location: Rome – Main Auditorium
Poster Presentations		
Evolution of Symptoms, Rate, and Rhythm Control Therapy in AF Patients in Europe: A Comparison of the PREFER in AF and PREFER in AF Prolongation Data Sets	Yanish Purmah, MD, City Hospital, Birmingham, United Kingdom	Sunday, August 28, 8:30 AM-12:30 PM CET Location: Poster Area
Insulin-requiring Versus Non-insulin Requiring Diabetes and Thromboembolic Risk in Patients with Atrial Fibrillation: A PREFER in AF Registry Sub-study	Elisabetta Ricottini, MD, University Campus Bio-Medico, Rome, Italy	Sunday, August 28, 2:00-6:00 PM CET Location: Poster Area
Antithrombotic Management of Atrial Fibrillation:	Giulia Renda, MD, PhD,	Sunday, August 28,

Follow-up Data from the PREFER in AF Registry	G. d'Annunzio University of Chieti-Pescara, Chieti, Italy	2:00-6:00 PM CET Location: Poster Area
The HAS-BLED Score for Prediction of Stroke and Systemic Embolism: Insights from the PREvention oF thromboembolic events – European Registry in Atrial Fibrillation (PREFER in AF)	Miklos Rohla, MD, Medical University of Vienna, Vienna, Austria	Sunday, August 28, 2:00-6:00 PM CET Location: Poster Area
Patients' Convenience and Satisfaction as Important Factors Related to Switching from Vitamin K Antagonists to NOACs – A PREFER in AF Registry Analysis	Raffaele De Caterina, MD, PhD, FESC, G. d'Annunzio University of Chieti-Pescara Chieti, Italy	Sunday, August 28, 2:00-6:00 PM CET Location: Poster Area
Moderated Poster Presentation		
Hospitalization-Related Costs Among Patients with Atrial Fibrillation Treated with the Factor Xa Inhibitor Edoxaban vs Warfarin: Results from the ENGAGE AF-TIMI 48 Trial	Elizabeth A. Magnuson, ScD, Saint Lukes Hospital, Kansas City, Missouri, United States of America	Tuesday, August 30, 10:25-10:35 AM CET Location: Moderated Poster Station – Poster Area
Rapid Fire Abstracts		
Linking Intrinsic Factor X Activity, a Biologically Relevant Pharmacodynamic Marker, to Edoxaban Plasma Concentration and Clinical Outcomes in the ENGAGE AF-TIMI 48 Trial	Ophelia Q. Yin, Phd, FCP, Daiichi Sankyo, Edison, New Jersey, United States of America	Sunday, August 28, 11:36-11:45 AM CET Location: Agora 1 – Poster Area
Gender Differences in Clinical Presentation and Predictors of One-Year Outcomes in Atrial Fibrillation	Renate B. Schnabel, MD, MSc, University Heart Center Hamburg, Hamburg, Germany	Monday, August 29, 9:15-9:24 AM CET Location: Agora 1 – Poster Area
Relationship Between Body Mass Index and Outcomes in 21,028 Patients with Atrial Fibrillation Treated with Edoxaban or Warfarin in ENGAGE AF-TIMI 48 Trial	Giuseppe Boriani, MD, PhD, University of Modena, Modena, Italy	Tuesday, August 30, 2:09-2:18 PM CET Location: Agora 2 – Poster Area
Management of Acute Venous Thromboembolism in Europe - Follow-up Data at 1 Month from the PREFER in VTE Registry	Rupert Bauersachs, MD, Max Ratschow Clinic for Angiology, Darmstadt, Germany	Tuesday, August 30, 5:06-5:15 PM CET Location: Galileo – The Hub
Young Investigator Awards Presentations		
Clinical Events After Interruption of Anticoagulation in Patients With Atrial Fibrillation: A Subgroup Analysis From the ENGAGE AF-TIMI 48 Trial	Ilaria Cavallari, MD, Brigham and Women's Hospital, Boston, Massachusetts, United States of America	Sunday, August 28, 12:57-1:15 PM CET Location: Raphael – The Hub
A Novel Risk Prediction Score in Atrial Fibrillation for a Net Clinical Outcome from the ENGAGE AF-TIMI 48 Randomized Clinical Trial	Christina Fanola, MD, Boston Medical Center, Brookline, Boston, Massachusetts, United States of America	Sunday, August 28, 1:32-1:50 PM CET Location: Galileo - The Hub

About ENSURE-AF

(**E**doxaba**N** vs. warfarin in subject**S U**nde**R**going cardiov**E**rsion of **A**trial **F**ibrillation)

ENSURE-AF is a **P**rospective, **R**andomized, **O**pen-Label, **B**linded **E**ndpoint evaluation (PROBE), parallel-group phase 3b study, evaluating the efficacy and safety of once-daily edoxaban versus enoxaparin/warfarin in patients with NVAF undergoing electrical cardioversion. The primary efficacy endpoint was the composite of stroke, systemic embolism, myocardial infarction, and cardiovascular mortality. The primary safety endpoint was the composite of major and clinically-relevant non-major bleeding. A total of 2,199 NVAF patients undergoing electrical cardioversion were enrolled at 239 clinical sites across North America and Europe. Patients were randomized to receive edoxaban 60 mg (or a reduced dose of edoxaban 30 mg for specific patients with renal impairment or low body weight or P-glycoprotein inhibitor use) or enoxaparin/warfarin for 28-49 days.[1]

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 at moderate-to-high risk of thromboembolic events. 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 in comparison to warfarin. For the principal safety endpoint, edoxaban was found to significantly reduce major bleeding compared to warfarin.[2]

About PREFER in AF

The initial PREFER in AF registry enrolled 7,243 AF patients across 461 centres in Austria, France, Germany, Italy, Spain, Switzerland and the UK. The aim of this registry is to provide information on the characteristics and management of patients with AF with focus on prevention of thromboembolic events, specifically stroke, together with other important patient-focused considerations such as management, quality of life and treatment satisfaction of patients with AF.[3]

The Prolongation of PREFER in AF Registry was designed to extend the ongoing PREFER in AF registry to gain further insights on AF management. The extension to the PREFER in AF registry includes two additional countries (Belgium and the Netherlands). Data is being collected from 5,000 patients across 325 centres in the nine European countries.[4]

About PREFER in VTE
The PREFER in VTE registry enrolled patients in seven European countries, including Austria, France Germany, Italy, Spain, Switzerland, and the UK to assess the real-life acute mid-term management of patients with VTE, the use of healthcare resources, and to provide data to estimate the costs for 12 months of treatment following a first-time and/or recurrent VTE diagnosis. In addition, PREFER in VTE is the first registry of its kind to capture comprehensive real-world data regarding quality of life, patient satisfaction and the economic burden of VTE treatment across Europe.[5]

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.[6]

AF is the most common type of heart rhythm disorder, and is associated with substantial morbidity and mortality.[7] AF affects approximately 6.1 million people in the U.S.[8] Compared to those without AF, people with the arrhythmia have a 3-5 times higher risk of stroke.[9] One in five of all strokes are as a result of AF.[10]

About VTE
VTE is an umbrella term for two conditions, deep vein thrombosis (DVT) and pulmonary embolism (PE). DVT is a disease caused by a blood clot found in deep veins, usually within the lower leg, thigh or pelvis, although they can occur in other parts of the body as well.[11] PE occurs when part of a clot detaches and lodges in the pulmonary arteries, causing a potentially fatal condition.[12]

VTE is a major cause of morbidity and mortality.[13] In the U.S., it is estimated that more than 950,000 VTE events and approximately 300,000 VTE related deaths occur each year.[14,15] There is a high rate of recurrence after a first VTE event, which is reduced with anticoagulant treatment. Without anticoagulant treatment, approximately half of patients who experience an initial VTE event have recurrent VTE within three months.[16]

About Edoxaban
Edoxaban is an oral, once-daily, direct factor Xa (pronounced "Ten A") inhibitor. Factor Xa is one of the key components in the coagulation cascade responsible for blood clotting. Inhibition of factor Xa reduces thrombin generation, prolongs clotting time and reduces the risk of thrombus formation.

About SAVAYSA® (edoxaban)
Edoxaban, also known as SAVAYSA in the U.S., is an oral, once-daily anticoagulant that specifically inhibits factor Xa, which is an important factor in the coagulation system that leads to blood clotting. The global edoxaban clinical trial program included two phase 3 clinical studies, Hokusai-VTE and ENGAGE AF-TIMI 48, with nearly 30,000 patients combined. The results from these trials formed the basis of the regulatory filing in the U.S. for SAVAYSA for the reduction in risk of stroke and systemic embolism (SE) in patients with non-valvular atrial fibrillation (NVAF), as well as for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) following 5-10 days of initial therapy with a parenteral anticoagulant. According to the U.S. label, SAVAYSA should not be used in NVAF patients with creatinine clearance (CrCL) levels greater than 95 mL/min because in that population there is an increased risk of ischemic stroke compared to warfarin.

Indication
SAVAYSA® (edoxaban) is a prescription medicine used to reduce the risk of stroke and blood clots in people who have atrial fibrillation not caused by a heart valve problem. Based on how well the kidneys work, SAVAYSA may not be a treatment option. Health Care Professionals should check kidney function before starting treatment.

SAVAYSA is used to treat blood clots in the veins of the legs (deep vein thrombosis) or lungs (pulmonary embolism), after treatment with an injectable blood thinner medicine for 5 to 10 days.

Important Safety Information

What is the most important information to know about SAVAYSA?

- **For people who take SAVAYSA for nonvalvular atrial fibrillation (a type of irregular heartbeat):** People with atrial fibrillation are at an increased risk of forming a blood clot in the heart, which can travel to the brain, causing a stroke, or to other parts of the body. SAVAYSA lowers the chance of having a stroke by helping to prevent clots from forming.

  Health Care Professionals should check kidney function before prescribing SAVAYSA. People whose kidneys work really well should not receive SAVAYSA because it may not work as well as other medications to prevent stroke.

  Patients should not stop taking SAVAYSA without first talking to their doctor who prescribed it.
  Stopping SAVAYSA increases the patient's risk of having a stroke.

- **SAVAYSA can cause bleeding which can be serious,** and sometimes lead to death. This is because SAVAYSA is a blood thinner medicine that reduces blood clotting. While taking SAVAYSA, the patient may bruise more easily and bleeding may take longer to stop. Patients should call their doctor or get medical help right away if they experience bleeding that is severe (for example, coughing up or vomiting blood) or bleeding that cannot be controlled.

  Patients may have a higher risk of bleeding if they take SAVAYSA and take other medicines that increase their risk of bleeding, including: aspirin, long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs), and blood thinners (warfarin, heparin, or other medicines to prevent or treat blood clots). Patients should tell their doctor if they take any of these medicines. Patients should ask their doctor or pharmacist if they are not sure if their medicine is one listed above.

- **SAVAYSA is not for people with mechanical heart valves or people who have moderate-to severe narrowing (stenosis) of their mitral valve.**

- **Spinal or epidural blood clots (hematoma).** People who take a blood thinner medicine (anticoagulant) like SAVAYSA, and have medicine injected into their spinal and epidural area, or have a spinal puncture have a risk of forming a blood clot that can cause long-term or permanent loss of the ability to move (paralysis). The risk of developing a spinal or epidural blood clot is higher if: a thin tube called an epidural catheter is placed in the patient's back to give him/her certain medicine, the patient takes NSAIDs or a medicine to prevent blood from clotting, the patient has a history of difficult or repeated epidural or spinal punctures, and the patient has a history of problems with his/her spine or has had surgery on his/her spine.

  If a patient takes SAVAYSA and receives spinal anesthesia or has a spinal puncture, the patient's doctor should watch closely for symptoms of spinal or epidural blood clots. Patients should tell their doctor right away if they have back pain, tingling, numbness (especially in the legs and feet), muscle weakness, loss of control of the bowels or bladder (incontinence).

Who should not take SAVAYSA?

Patients should not take SAVAYSA if they currently have certain types of abnormal bleeding.

What should patients tell their doctor before taking SAVAYSA?

- Before taking SAVAYSA, patients should tell their doctor if they: have liver or kidney problems, have ever had bleeding problems, have a mechanical heart valve, are pregnant or plan to become pregnant, are breastfeeding or plan to breastfeed.

  It is not known if SAVAYSA will harm an unborn baby. Patients should tell their doctor right away if they become pregnant during treatment with SAVAYSA.

  It is not known if SAVAYSA passes into breast milk. Patients should decide with their doctor if they will take SAVAYSA or breastfeed. Patients should not do both.

- Patients should tell all of their doctors and dentists that they are taking SAVAYSA. The health care providers should talk to the doctor who prescribed SAVAYSA before the patient has any surgery, medical or dental procedure. Patients should tell their doctor about all the medicines they take, including prescription and over-the-counter medicines,

vitamins, and herbal supplements. Some other medicines may affect the way SAVAYSA works. Certain medicines may increase the risk of bleeding or stroke when taken with SAVAYSA.

How should the patient take SAVAYSA?

- Patients should take SAVAYSA exactly as prescribed. The doctor will decide how long the patient should take SAVAYSA. The patient should not change their dose or stop taking SAVAYSA unless their doctor tells them to.

  Patients can take SAVAYSA with or without food. If a dose of SAVAYSA is missed, the patient should take it as soon as he/she remembers that day and not take more than one dose at the same time. The next dose should be taken at the usual time the next day. Patients should not run out of SAVAYSA and should refill their prescriptions before running out.

- If too much SAVAYSA is taken, the patient should go to the nearest hospital emergency room or call his/her doctor right away. Patients should call their doctor right away if they fall or injure themselves, especially if they hit their heads. The doctor may need to check them.

What are the possible side effects of SAVAYSA?

Common side effects in people who take SAVAYSA include bleeding and low red blood cell count (anemia). Patients should talk to their doctor if they have any side effect that bothers them or that does not go away. Patients should call their doctor for medical advice about side effects. Side effects may be reported to FDA at 1-800-FDA-1088.

Please see the full Prescribing Information, including **Boxed WARNINGS** and Medication Guide at savaysa.com.

Edoxaban is currently marketed in South Korea, the Netherlands, Ireland, the UK, Germany, Switzerland, the US and Japan, and was approved in Taiwan. In other countries, regulatory review is ongoing.

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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