

For Immediate Release

Company name: DAIICHI SANKYO COMPANY, LIMITED  
Representative: Takashi Shoda, President and Representative Director  
(Code no.: 4568, First Section, Tokyo, Osaka and Nagoya Stock Exchanges)  
Please address inquiries to Toshiaki Sai, General Manager,  
Corporate Communications Department  
Telephone: +81-3-6225-1126  
<http://www.daiichisankyo.com/>

**NEW PHASE II DATA SHOW SAFETY OF ONCE-DAILY ORAL  
FACTOR Xa INHIBITOR, DU-176b, COMPARABLE TO WARFARIN IN PATIENTS  
WITH NON-VALVULAR ATRIAL FIBRILLATION**

**DAIICHI SANKYO INITIATES PHASE III TRIAL OF ITS INVESTIGATIONAL  
FACTOR Xa INHIBITOR, DU-176b, IN PATIENTS WITH ATRIAL FIBRILLATION**

*ENGAGE-AF TIMI 48 Trial to Study 16,500 Patients in More than 1,400 Centers Globally*

These attached are the press releases, which were issued in US on December 7, 2008.  
(US time)



**Daiichi-Sankyo**

For more information, please contact:

Toshiaki Sai  
Daiichi Sankyo Company, Limited (Tokyo)  
Phone: +81-3-6225-1126

Dr. Felix Münzel  
Daiichi Sankyo Europe GmbH  
Phone + 49-(0)-89-7808-471

Kimberly Wix  
Daiichi Sankyo, Inc. (United States)  
Phone: +1 (973) 695-8338  
Mobile : +1 (908) 656-5447

Dr. Thomas Portz  
Daiichi Sankyo Europe GmbH  
Phone: + 49 (0)89-78 08 468  
Mobile: + 49 (0)172-841 5904

**EMBARGOED UNTIL: December 7, 2008 at 9:30 a.m. PST**  
**Abstract Number: 33**

**NEW PHASE II DATA SHOW SAFETY OF ONCE-DAILY ORAL  
FACTOR Xa INHIBITOR, DU-176b, COMPARABLE TO WARFARIN IN PATIENTS  
WITH NON-VALVULAR ATRIAL FIBRILLATION**

**SAN FRANCISCO, December 7, 2008** – Patients with non-valvular atrial fibrillation receiving either 30 mg or 60 mg once-daily dose of DU-176b, an investigational oral Factor Xa inhibitor, experienced comparable safety and tolerability compared to those taking warfarin, according to new Phase II data presented today at the 50<sup>th</sup> Annual Meeting of the American Society of Hematology in San Francisco. These findings are the first results from a clinical study evaluating an oral Factor Xa inhibitor in atrial fibrillation patients. DU-176b is being developed solely by Daiichi Sankyo Company, Limited (TSE: 4568).

The objective of the multinational study was to assess the safety of four dose regimens of DU-176b in patients with non-valvular atrial fibrillation (AF), as compared to warfarin. While the incidence of major and clinically relevant non-major bleeding events was significantly higher in the twice-daily DU-176b treatment groups (30 mg or 60 mg twice per day), compared with warfarin, the incidence reported in the once-daily DU-176b

treatment groups (30 mg or 60 mg once per day) was similar to that in the warfarin-treated patient group. Bleeding events were evaluated using guidelines established by the International Society on Thrombosis and Haemostasis<sup>1</sup>, the most sensitive scale of those currently used in clinical studies in cardiovascular disease.

“These results are noteworthy and encouraging because we observed significantly fewer adverse bleeding events in patients receiving one dose of DU-176b per day, versus two doses per day, suggesting with this compound, the most convenient dosing regimens also appear to be safer,” said Jeffrey I. Weitz, MD, FACP, FRCP, professor of medicine and biochemistry, McMaster University and director, Henderson Research Centre, Hamilton, Ontario. “These data provide insight into the optimal dosing regimens for Phase III studies of DU-176b.”

“Having clear results from a robust Phase II study among atrial fibrillation patients gives us confidence in evaluating the doses selected for our Phase III clinical trial,” said Francis Plat, M.D., vice president, clinical development at Daiichi Sankyo Pharma Development. “We are hopeful that DU-176b may one day provide the community a safe and convenient treatment in the prevention of stroke in patients with non-valvular atrial fibrillation.”

#### **About the DU-176b Phase II Safety Study:**

A total of 1,146 patients with atrial fibrillation with a CHADS<sub>2</sub> index  $\geq 2$  were enrolled in the study. Patients were randomly assigned to receive either one of the four fixed dose regimens of DU-176b (30mg/N=235 or 60mg/N=234 administered once daily; 30mg/N=244 or 60mg/N=180 administered twice daily), or warfarin (N=250) dose-adjusted locally to a target international normalized ratio (INR) of 2.0-3.0 for 12 weeks. The INR was determined weekly for four weeks and every two weeks thereafter. Investigators, sponsors and study subjects were blinded to the DU-176b dose; however, those taking warfarin were aware they were randomized to the warfarin arm.

The primary endpoints of the study were the incidence of bleeding events (major and clinically relevant non-major) and elevated liver enzymes and/or bilirubin. Secondary endpoints included major adverse cardiovascular events, stroke, systemic embolism, acute myocardial infarction, hospitalizations due to cardiovascular conditions or cardiovascular death.

---

<sup>1</sup>Schulman S., et al. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *Journal of Thrombosis and Haemostasis* 2005;3: 692–694.

The incidence of major and clinically relevant non-major bleeding events was significantly higher with the 30 mg and 60 mg twice-daily DU-176b regimens (7.8 percent,  $p = 0.029$  and 10.6 percent,  $p = 0.002$  respectively) than it was in patients given warfarin (3.2 percent). In contrast, the incidence of major and clinically relevant non-major bleeding events with the 30 and 60 mg once-daily DU-176b regimens was comparable to that with warfarin (3.0 percent, 3.8 percent and 3.2 percent, respectively). There were no significant differences in the numbers of patients with elevated liver enzymes or bilirubin across all treatment groups. Although the study was not powered to detect efficacy, there were no significant differences in the rates of secondary endpoints across treatment groups.

### **About Atrial Fibrillation**

Atrial fibrillation is an irregular heartbeat caused when the upper chambers of the heart (the atria) beat inconsistently and rapidly. When this happens, blood can become stagnant near the walls of the atria and form blood clots. These blood clots can break off and travel through the blood stream to the brain where they can plug blood vessels possibly causing a stroke. These clots can also cause damage to other organs in the body by blocking peripheral arteries.

Approximately 90,000 strokes in the U.S result from atrial fibrillation.<sup>2</sup> Patients with atrial fibrillation have five times higher risk of having a stroke.<sup>3</sup> These patients also tend to have more serious first strokes than those without atrial fibrillation, resulting in higher mortality rates and longer hospital stays.<sup>1</sup>

### **About DU-176b**

DU-176b is an oral anticoagulant that directly inhibits Factor Xa, a clotting factor in the blood. Daiichi Sankyo is developing DU-176b as a potential new treatment for the prevention of both arterial and venous thromboembolism. Notably, Daiichi Sankyo has more than 25 years experience conducting research in the area of Factor Xa inhibition and was the first company to test these compounds in humans.

---

<sup>2</sup> Jorgensen, H.S., Nakayama, H, Reith, J. et. al. Acute stroke with atrial fibrillation. *Stroke* 1996;27: 1765-1769.

<sup>3</sup> Hylek AM, et al. *N Engl J Med.* 2003; 349:1019-1026.

## **About Daiichi Sankyo**

A global pharma innovator, Daiichi Sankyo Co., Ltd., was established in 2005 through the merger of two leading Japanese pharmaceutical companies. This integration created a more robust organization that allows for continuous development of novel drugs that enrich the quality of life for patients around the world. A central focus of Daiichi Sankyo's research and development are thrombotic disorders, malignant neoplasm, diabetes mellitus, and autoimmune disorders. Equally important to the company are hypertension, hyperlipidemia or atherosclerosis and bacterial infections. For more information, visit [www.daiichisankyo.com](http://www.daiichisankyo.com).

Daiichi Sankyo, Inc., headquartered in Parsippany, New Jersey, is the U.S. subsidiary of Daiichi Sankyo Co., Ltd. For more information on Daiichi Sankyo, Inc., please visit [www.dsus.com](http://www.dsus.com).

### **Forward-Looking Statements**

*This news release may contain forward-looking statements based on current assumptions and forecasts made by Daiichi Sankyo group. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in our public reports, which are available on the website at [www.daiichisankyo-us.com](http://www.daiichisankyo-us.com). The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.*

# # #



**Daiichi-Sankyo**

For more information, please contact:

Toshiaki Sai  
Daiichi Sankyo Company, Limited (Tokyo)  
Phone: +81-3-6225-1126

Dr. Felix Münzel  
Daiichi Sankyo Europe GmbH  
Phone + 49-(0)-89-7808-471

Kimberly Wix  
Daiichi Sankyo, Inc. (United States)  
Phone: +1 (973) 695-8338  
Mobile : +1 (908) 656-5447

Dr. Thomas Portz  
Daiichi Sankyo Europe GmbH  
Phone: + 49 (0)89-78 08 468  
Mobile: + 49 (0)172-841 5904

**DAIICHI SANKYO INITIATES PHASE III TRIAL OF ITS INVESTIGATIONAL  
FACTOR Xa INHIBITOR, DU-176b, IN PATIENTS WITH ATRIAL FIBRILLATION**

*ENGAGE-AF TIMI 48 Trial to Study 16,500 Patients in More than 1,400 Centers Globally*

**Tokyo, Japan and Edison, N.J. – December 7, 2008** – Daiichi Sankyo Company, Limited (TSE: 4568), announced today that it has initiated its pivotal Phase III trial for DU-176b, an investigational oral Factor Xa inhibitor, in patients with atrial fibrillation. DU-176b is being developed solely by Daiichi Sankyo.

The Phase III global study, Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation (ENGAGE-AF), will compare DU-176b with warfarin in preventing stroke and systemic embolic events (SEE) in patients with atrial fibrillation. The primary safety assessment will be the incidence of bleeding.

Results from a recently presented Phase II safety study showed that the incidence of major and clinically relevant non-major bleeding events reported in the once-daily DU-176b treatment groups (30 mg or 60 mg) was similar to that in the warfarin-treated patient group. The incidence of major and clinically relevant non-major bleeding events was significantly higher in the twice-daily DU-176b treatment groups (30 mg or 60 mg), compared to the warfarin group. The Phase III study will therefore randomize approximately 16,500 patients to one of three treatment groups: 30 mg DU-176b once

daily, 60 mg DU-176b once daily, or warfarin. Those randomized to warfarin will be dosed once daily with dose adjustments to maintain International Normalized Ratio (INR) between 2.0 and 3.0.

This is an event-driven, Phase III, multinational, randomized, double-blind study with sites in North and South America, Africa, Asia, Europe, Australia and New Zealand. The expected median treatment duration of the study is 24 months; Daiichi Sankyo expects the study to conclude in the first half of 2012.

“There is a need for a safe and effective option for the prevention of clotting or stroke in patients with atrial fibrillation other than the current standard of care, warfarin, which requires extensive monitoring and poses potentially serious drug and food interactions,” said John Alexander, M.D., M.P.H., global head of research and development, Daiichi Sankyo Company, Limited. “The start of our Phase III trial marks an important milestone in the clinical development of DU-176b and we hope this compound will prove to be another successful treatment in our cardiovascular portfolio.”

### **About Atrial Fibrillation**

Atrial fibrillation (AF) is an irregular heartbeat caused when the upper chambers of the heart (the atria) beat inconsistently and rapidly. When this happens, blood can become stagnant near the walls of the atria and form blood clots. These blood clots can break off and travel through the blood stream to the brain where they can block blood vessels possibly causing a stroke. These clots can also cause damage to other organs in the body by blocking peripheral arteries.

About 90,000 strokes in the U.S. are caused by atrial fibrillation.<sup>2</sup> Patients with atrial fibrillation have five times higher risk of having a stroke.<sup>3</sup> These patients also tend to have more serious first strokes than patients without atrial fibrillation, resulting in higher mortality rates and longer hospital stays.<sup>1</sup>

### **About DU-176b**

DU-176b is an oral anticoagulant that directly inhibits Factor Xa, a clotting factor in the blood. Daiichi Sankyo is developing DU-176b as a potential new treatment for the prevention of both arterial and venous thromboembolism. Notably, Daiichi Sankyo has more than 25 years experience conducting research in the area of Factor Xa inhibition and was the first company to test these compounds in humans.

## **About Daiichi Sankyo**

A global pharma innovator, Daiichi Sankyo Co., Ltd., was established in 2005 through the merger of two leading Japanese pharmaceutical companies. This integration created a more robust organization that allows for continuous development of novel drugs that enrich the quality of life for patients around the world. A central focus of Daiichi Sankyo's research and development are thrombotic disorders, malignant neoplasm, diabetes mellitus, and autoimmune disorders. Equally important to the company are hypertension, hyperlipidemia or atherosclerosis and bacterial infections. For more information, visit [www.daiichisankyo.com](http://www.daiichisankyo.com).

Daiichi Sankyo, Inc., headquartered in Parsippany, New Jersey, is the U.S. subsidiary of Daiichi Sankyo Co., Ltd. For more information on Daiichi Sankyo, Inc., please visit [www.dsus.com](http://www.dsus.com).

### **Forward-Looking Statements**

*This news release may contain forward-looking statements based on current assumptions and forecasts made by Daiichi Sankyo group. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in our public reports, which are available on the website at [www.daiichisankyo-us.com](http://www.daiichisankyo-us.com). The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.*

# # #