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Study Shows More Potent and More Reliable Platelet Inhibition with Prasugrel Compared to Clopidogrel Even in Patients With More Reactive Platelets

INDIANAPOLIS and TOKYO, March 14, 2006 /PRNewswire-FirstCall via COMTEX News Network/ -- In early phase data announced today, the investigational antiplatelet agent, prasugrel, demonstrated greater and more reliable antiplatelet effect compared to clopidogrel (Plavix(R)) even in patients with increased platelet reactivity. These data were featured in one of several prasugrel presentations at the 2006 Scientific Sessions of the American College of Cardiology in Atlanta.

In a Phase Ib study, greater than 90 percent of prasugrel-treated patients achieved greater than 20 percent inhibition of platelet aggregation (IPA), compared with less than 50 percent of clopidogrel-treated patients. The study showed that even patients with more reactive platelets at baseline, a population whose platelets may be less affected or unaffected by current thienopyridine therapies, have higher and more consistent inhibition of platelet aggregation with prasugrel than with clopidogrel.

"Certain patients have more reactive platelets that are less affected or unaffected by current thienopyridines, so it is very encouraging to see in this study how well the platelets of those who were dosed with prasugrel responded, regardless of baseline platelet reactivity," said Joseph Jakubowski, PhD, Research Fellow, Eli Lilly and Company.

In a second study, prasugrel was shown to produce rapid, potent, and consistent inhibition of both platelet activation and generation of thrombo- inflammatory markers. Notably, the inhibitory effect of prasugrel was independent of the effects of aspirin. Moreover, the study results suggest that pre-treatment with aspirin is not required for prasugrel blockade of ADP-induced platelet activation.

"In our study, prasugrel demonstrates important qualities that clinicians seek in an antiplatelet therapy," said lead study investigator Andrew Frelinger, PhD, Associate Director of the Center for Platelet Function Studies and Research Associate Professor of Pediatrics and Molecular Genetics & Microbiology at the University of Massachusetts Medical School, Worcester, MA. "We hope that the ability of prasugrel to quickly and effectively inhibit platelet aggregation, by mechanisms distinct from and complementary to aspirin, will translate into improved clinical outcomes in future trials."

Eli Lilly and Company (NYSE: LLY) and Sankyo Company Ltd., a subsidiary of Daiichi Sankyo Company, Limited (TSE: 4568) are developing prasugrel, an oral antiplatelet agent, as a potential treatment for patients who have suffered a heart attack or unstable angina (heart-related chest pain). Antiplatelet agents are used both acutely and as maintenance therapy to inhibit platelet activation and aggregation that occur in diseased arteries and in response to invasive procedures such as percutaneous coronary intervention (PCI), a procedure to open blockages in heart arteries, that includes the use of coronary stents. Antiplatelet agents prevent platelets from clumping or sticking together, which can cause formation of blood clots and lead to heart attack or stroke. Recent studies suggest that a relationship may exist between a poor platelet response to antiplatelet agents in individual patients and poor clinical outcomes, which manifest as major adverse cardiovascular events, including heart attacks.(i,ii,iii)

About the Data

In the Phase Ib study, "The Influence of Baseline Platelet Aggregation Response on Subsequent Inhibition of Aggregation Achieved with Clopidogrel or Prasugrel" (Abstract 328), 81 aspirin-treated patients with stable cardiovascular disease were randomized to receive the approved 300 mg loading dose of clopidogrel or 40 or 60 mg of prasugrel. Inhibition of platelet aggregation and the change in maximum platelet aggregation (MPA) from baseline were evaluated six hours after the medication was administered. Greater than 90 percent of patients dosed with prasugrel achieved greater than 20 percent inhibition, compared with less than 50 percent of clopidogrel-treated patients.

In the second study, "The Active Metabolite of Prasugrel (CS-747) Inhibits ADP-Stimulated Thrombo-inflammatory Markers of Platelet Activation: Modulation by Other Blood Cells and Calcium, But Not by Aspirin" (Abstract 332), blood from nine healthy donors, pre- and post-aspirin treatment, was incubated with varying concentrations of the active metabolite of prasugrel. Adenosine diphosphate (ADP) was used to induce platelet activation and aggregation in samples of subjects' blood.

Platelets from all subjects responded to prasugrel, which produced rapid, potent and consistent inhibition of platelets independent of the presence of aspirin. A high concentration of the active metabolite of prasugrel (10 micromolar) completely

inhibited platelet aggregation in approximately one minute, and a 10-fold lower concentration (1 micromolar) reached maximal effect between 15 and 30 minutes. Thrombo-inflammatory markers such as platelet surface P-selectin and monocyte-platelet aggregates also showed rapid and potent dose-inhibition by prasugrel.

Current Clinical Research with Prasugrel

A Phase III clinical study with prasugrel -- TRITON-TIMI 38 -- is under way. This head-to-head study will compare the effects of prasugrel with clopidogrel in up to 13,000 patients with acute coronary syndrome who suffer a heart attack or have unstable angina and are to undergo PCI. It is anticipated that the TRITON-TIMI 38 study should be completed in early 2007 with regulatory submissions to follow in the second half of 2007.

"The results from our early studies suggest that prasugrel has the potential to be a highly effective antiplatelet therapy," said Francis Plat, MD, Vice President, Clinical Development - Cardiovascular, Sankyo Pharma Inc. "Our pivotal Phase III trial will demonstrate whether the unique attributes of prasugrel translate into improved clinical outcomes for patients."

Cardiovascular disease is the leading cause of death in the U.S. and worldwide, killing 17 million people each year.(iv) Acute heart attacks and unstable angina, called acute coronary syndrome (ACS), affect more than 942,000 Americans each year. Despite current medical interventions, 300,000 people experience recurrent heart attacks and 500,000 people die from heart attacks annually in the U.S.(v)

About Prasugrel

Prasugrel is an investigational antiplatelet agent designed to prevent platelet activation and aggregation by blocking adenosine diphosphate receptors on the platelet surface. This novel oral compound was discovered by Sankyo and Ube Industries, Ltd. (TSE: 4208). It is being investigated as a potential treatment for higher-risk patients with acute coronary syndrome who undergo PCI.

About Lilly

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers -- through medicines and information -- for some of the world's most urgent medical needs. Building on the strong foundation of ReoPro (abciximab), Lilly is in the process of building a robust cardiovascular pipeline. Lilly has multiple cardiovascular drugs in that pipeline -- in every stage from pre-clinical and Phase I to the Phase III trials for prasugrel. Additional information is available at www.lilly.com. P-LLY

About Daiichi Sankyo Company, Limited

Daiichi Sankyo Company, Limited was established on Sept. 28, 2005, as the joint holding company of two major Japanese pharmaceutical companies -- Sankyo Co., Ltd., and Daiichi Pharmaceutical Co., Ltd. Daiichi Sankyo is a global pharmaceutical innovator, continuously generating innovative drugs and services and maximizing its corporate value. Sankyo and Daiichi Pharmaceutical have a broad range of major drug products on the Japanese market, including the antihypertensive Benicar(R) (olmesartan medoxomil) and the synthetic antibacterial agent Cravit(R) (levofloxacin). Both companies have used their cumulative knowledge and expertise in the field of cardiovascular disease as a foundation for developing an abundant product lineup and R&D pipeline. For further details, please refer to the company Web site at <http://www.daiichisankyo.co.jp/eng>.

This press release contains certain forward-looking statements about the potential of the investigational compound prasugrel (CS-747, LY640315) and reflects Lilly's current beliefs. However, as with any pharmaceutical product under development, there are substantial risks and uncertainties in the process of development and regulatory review. There is no guarantee that the product will receive regulatory approvals, or that the regulatory approval will be for the indication(s) anticipated by the company. There is also no guarantee that the product will prove to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filing with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

Plavix(R) is a registered trademark of Sanofi-Synthelabo Inc.

(i) Barragan, P., Bouvier, J. L., Roquebert, P. O., Macaluso, G., Commeau, P., Comet, B., Lafont, A., Camoin, L., Walter, U., and Eigenthaler, M. Resistance to thienopyridines: clinical detection of coronary stent thrombosis by monitoring of vasodilator-stimulated phosphoprotein phosphorylation. *Catheter Cardiovasc Interv* 2003; 59: 295-302

(ii) Muller, I., Besta, F., Schulz, C., Massberg, S., Schonig, A., and Gawaz, M. Prevalence of clopidogrel non-responders among patients with stable angina pectoris scheduled for elective coronary stent placement. *Thromb Haemost* 2003; 89: 783-787

(iii) Matetzky, S., Shenkman, B., Guetta, V., Shechter, M., Bienart, R., Goldenberg, I., Novikov, I., Pres, H., Savion, N., Varon, D., and Hod, H. Clopidogrel resistance is associated with increased risk of recurrent atherothrombotic events in patients with acute myocardial infarction. *Circulation* 2004; 109: 3171-3175.

(iv) World Health Organization. The Atlas of Heart Disease and Stroke - Types of Cardiovascular Disease 2005.

(v) American Heart Association. Heart Disease and Stroke Statistics 2005.

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