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**Refer to:** Christina D. Gaines, APR  
Eli Lilly and Company  
+1-317-276-3845 (office)  
+1-317-366-2568 (cell)

Michaela Paudler-Debus, PhD  
Daiichi Sankyo (Tokyo)  
+81-3-6225-1338 (office)  
+81 80 4359 9421 (cell)

**Daiichi Sankyo and Lilly Announce TRILOGY ACS Results Regarding Effient®  
(Prasugrel) in Acute Coronary Syndrome UA/NSTEMI Patients to be Managed  
Medically without an Artery-Opening Procedure**

*Study did not meet primary objective of demonstrating prasugrel superiority over  
clopidogrel in this patient population*

**INDIANAPOLIS, USA, TOKYO, JAPAN, August 26, 2012** – Daiichi Sankyo Company, Limited (TSE: 4568), and Eli Lilly and Company (NYSE: LLY) today announced data from the TRILOGY ACS study, a phase III trial comparing prasugrel plus aspirin to clopidogrel plus aspirin in patients with unstable angina (UA) or non-ST elevation myocardial infarction (NSTEMI), who were managed medically without an artery-opening procedure. At 30 months, 13.9 percent of prasugrel patients versus 16.0 percent of clopidogrel patients experienced the combined primary endpoint of heart attack, stroke or cardiovascular (CV) death in patients under 75 years of age, the primary analysis population (HR=0.91; 95% CI: 0.79-1.05).<sup>1</sup> This outcome was not statistically significant (P=0.21). Different from other large-scale trials, TRILOGY ACS

(TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medically manage Acute Coronary Syndromes) prospectively studied only the UA/NSTEMI population medically managed without revascularization (percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery).<sup>2</sup> Results of this study were published in the *New England Journal of Medicine* and also presented during a late-breaking session at the ESC Congress 2012 (European Society of Cardiology) in Munich, Germany.

From a safety perspective, TRILOGY ACS showed that rates of TIMI major bleeding events (including life-threatening or fatal bleeds) did not differ significantly between the prasugrel plus aspirin and clopidogrel plus aspirin treatment groups in patients less than 75 years of age or in the overall study population.<sup>1</sup> In patients under age 75, non-CABG TIMI major bleeding occurred in 2.1 percent of prasugrel patients versus 1.5 percent of clopidogrel patients (HR=1.31, 95% CI: 0.81-2.11, P=0.27).<sup>1</sup> However, the rates of TIMI major or minor bleeding were higher in patients treated with prasugrel (3.3 percent of prasugrel patients versus 2.1 percent of clopidogrel patients; HR=1.54; 95% CI: 1.06-2.23; P=0.02).<sup>1</sup>

“TRILOGY ACS was designed to evaluate dual oral antiplatelet therapy in UA/NSTEMI patients who are managed medically without revascularization,” said E. Magnus Ohman, M.D., Duke Clinical Research Institute and Chairperson of the TRILOGY ACS trial. “While the study did not demonstrate prasugrel was superior to clopidogrel in these patients, TRILOGY ACS provided some additional observations in this previously understudied population. The delayed treatment effect beyond 12 months observed in TRILOGY ACS had not been seen in earlier studies of shorter duration.”

An analysis performed to account for multiple recurrent ischemic events suggested a lower risk among participants <75 years treated with prasugrel (HR=0.85; 95% CI: 0.72-1.00; P=0.044).<sup>1</sup>

A post-hoc exploratory analysis observed a trend for a lower risk in heart attack, stroke and death among patients treated with prasugrel beyond one year; HRs and 95% CIs for the time period of <12 months versus the time period of >12 months comparing prasugrel versus clopidogrel for the primary efficacy endpoint were 0.99 (0.84-1.16) versus 0.72 (0.54-0.97) (interaction P=0.07).<sup>1</sup>

“Large-scale clinical trials in understudied populations, such as TRILOGY ACS, are important regardless of the result because they generate a sizeable amount of information for the medical community,” said J. Anthony Ware, M.D., Group Vice President and Cardiovascular/Acute Care Platform Leader, Eli Lilly and Company. “We look forward to presenting additional data from the platelet function sub-study, analyses of the elderly population data, as well as genomics information in future peer-reviewed forums.”

“While this is not the outcome we anticipated, we believe this study contributes to the knowledge base about ACS patients who are medically managed,” said Glenn Gormley, M.D., Ph.D., Global Head of Research & Development and Senior Executive Officer, Daiichi Sankyo Company, Limited. “The group of patients in the TRILOGY ACS trial is different from those who participated in the prior TRITON-TIMI 38 trial, where almost all ACS patients underwent percutaneous intervention.”

The TRILOGY ACS study was conducted by Daiichi Sankyo and Eli Lilly and Company in conjunction with the Duke Clinical Research Institute, one of the world’s leading academic clinical research organizations and a part of Duke University Medical Center in Durham, North Carolina, United States. Granted marketing authorization by the European Commission in February 2009, Efient<sup>®</sup> (prasugrel), co-administered with acetylsalicylic acid (ASA), is indicated for the prevention of atherothrombotic events in patients with acute coronary syndrome (ACS) (i.e. unstable angina, non-ST segment elevation myocardial infarction [UA/NSTEMI] or ST segment elevation myocardial infarction [STEMI]) undergoing primary or delayed percutaneous coronary intervention (PCI).<sup>3</sup> The Efient indication is based on the results of the TRITON-TIMI 38 trial.

## About TRILOGY ACS

TRILOGY ACS (TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medically manage Acute Coronary Syndromes) began in June 2008 and reached a total enrollment of 9,326 patients at more than 900 hospitals in 52 countries worldwide.<sup>2</sup>

TRILOGY ACS was a multi-center, double-blind, randomized, controlled trial to evaluate the safety and efficacy of prasugrel plus aspirin compared to clopidogrel plus aspirin in UA/NSTEMI patients who were to be medically managed without revascularization.<sup>2</sup> The primary endpoint was the time to occurrence of the first instance of the composite endpoint of CV death, heart attack or stroke.<sup>2</sup> The sample size in the trial was selected to detect a 22 percent relative risk reduction in patients treated for up to 30 months with prasugrel compared with clopidogrel.<sup>2</sup>

Inclusion criteria for the study included at least one of the following high-risk features in UA/NSTEMI patients: age greater than 60 years, prior myocardial infarction, diabetes mellitus, and/or prior revascularization (PCI or CABG).<sup>2</sup> Exclusion criteria included planned PCI or CABG, STEMI as the initial event, and medical management decision more than 72 hours after onset of event without clopidogrel treatment.<sup>2</sup>

Prasugrel loading and maintenance dosages in TRILOGY ACS were adjusted for the medically managed patient population enrolled and differ from the current indicated dosages for ACS-PCI patients.<sup>2</sup> Patients under the age of 75 and weighing more than 60 kg received a 10 mg maintenance dose of prasugrel. Prasugrel dosage adjustments (5 mg) were made for very elderly patients (75 years of age and older) and for those <60 kg; patients with prior TIA/stroke were excluded.<sup>2</sup>

The current prasugrel indication in ACS patients intended for planned PCI, is a single 60 mg loading dose (LD) followed by a once-daily 10 mg maintenance dose (MD).<sup>3</sup> A single 60 mg loading dose of prasugrel followed by a maintenance dose of prasugrel at a 5 mg once daily dose, co-administered with aspirin, should be used in lower weight patients (<60 kg) with ACS-PCI.<sup>3</sup>

Safety endpoints evaluated included bleeding as measured by GUSTO and TIMI criteria; plus systematic collection of neoplasm data (all suspected events to be adjudicated by an Oncology Clinical End Point Committee).<sup>2</sup>

More than 90 percent of the patients in the study were treated with clopidogrel prior to randomization, per the guidelines for secondary prevention.<sup>1</sup> Although all patients in the study were committed to be treated medically without revascularization for the index event, a small percentage of patients less than 75 years of age underwent revascularization (7.9 percent) after randomization.<sup>1</sup>

More information on the TRILOGY ACS trial and its design is available at:  
<http://clinicaltrials.gov/ct2/show/NCT00699998>.

### **About prasugrel**

Daiichi Sankyo Company, Limited, and Eli Lilly and Company co-developed prasugrel, an oral antiplatelet agent discovered by Daiichi Sankyo and its Japanese research partner, Ube Industries, Ltd. Prasugrel helps keep blood platelets from clumping together and developing a blockage in an artery. The European Commission granted marketing authorization for prasugrel for the prevention of atherothrombotic events in patients with ACS undergoing PCI, in combination with aspirin, in 2009.<sup>3</sup> To date prasugrel has been approved in more than 65 countries worldwide.

## **About Acute Coronary Syndromes**

Acute coronary syndrome includes heart attacks and unstable angina (UA, chest pain). Heart attack is a major manifestation of coronary heart disease (CHD), which occurs when the arteries become narrowed or clogged by cholesterol and fat deposits. In some cases the plaque can rupture, resulting in a blood clot which may partially or totally block the blood supply to portions of the heart, resulting in ACS.<sup>4</sup> There are two main types of heart attack: Non-ST-segment elevation, or NSTEMI, and ST-segment elevation, or STEMI.<sup>4</sup> STEMI heart attacks are often considered more severe as the artery is often fully blocked, preventing blood flow to the heart.

CHD is the single most common cause of death in the European Union, accounting for more than 741,000 deaths in the EU each year.<sup>5</sup> ACS affects more than one million people in the United States annually.<sup>6</sup> In Korea, the total number of ACS events rose by 70 percent in just five years (2004 – 2009).<sup>7</sup>

Many ACS patients undergo PCI to re-open the artery, which usually includes a stent placement. The number of UA or NSTEMI ACS patients worldwide who are managed without acute coronary interventions, such as PCI, has ranged from 32 percent to almost 60 percent over the last few years.<sup>8,9</sup> In many cases, these ACS patients may have complex coronary anatomy, comorbidities or other high-risk factors that prevent PCI or surgical intervention.<sup>9</sup>

## **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](http://www.daiichisankyo.com).

## About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of 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. Additional information about Lilly is available at [www.lilly.com](http://www.lilly.com).

*This press release contains certain forward-looking statements about prasugrel in acute coronary syndrome UA/NSTEMI patients to be managed medically without an artery-opening procedure and reflects Daiichi Sankyo's and Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is no guarantee that future study results and patient experience will be consistent with study findings to date or that the product will meet our commercial expectations. For further discussion of these and other risks and uncertainties, see Lilly's filing with the United States Securities and Exchange Commission and Daiichi Sankyo's filings with the Tokyo Stock Exchange. Daiichi Sankyo and Lilly undertake no duty to update forward-looking statements.*

Effient® is a registered trademark of Eli Lilly and Company.

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<sup>1</sup> Roe MT, Armstrong PW, Fox KAA, et al. Prasugrel versus Clopidogrel for Acute Coronary Syndromes without Revascularization. *N Engl J Med*. Published online August 26, 2012. DOI: 10.1056/NEJMoa1205512.

<sup>2</sup> Chin CT, Row MT, Fox KAA, et al. Study design and rationale of a comparison of prasugrel and clopidogrel in medically managed patients with unstable angina/non-ST-segment elevation myocardial infarction: The TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medically manage Acute Coronary Syndromes (TRILOGY ACS) trial. *Am Heart J*. 2010;160:16-22.

<sup>3</sup> European Medicines Agency. Effient Summary of Product Characteristics. Electronic Medicines Compendium website. Available at: [www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Product\\_Information/human/000984/WC500021971.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000984/WC500021971.pdf). Accessed August 2012.

<sup>4</sup> WebMD Medical Reference in Collaboration with the Cleveland Clinic. Heart Disease: Coronary Artery Disease. Available at: [www.webmd.com/heart-disease/guide/heart-disease-coronary-artery-disease](http://www.webmd.com/heart-disease/guide/heart-disease-coronary-artery-disease). Accessed May 2012.

<sup>5</sup> British Heart Foundation Health Promotion Research Group. European Cardiovascular Disease Statistics 2008. Available at: [www.bhf.org.uk/research/statistics.aspx](http://www.bhf.org.uk/research/statistics.aspx). Accessed May 2012.

<sup>6</sup> Roger VL, Go AS, Lloyd-Jones DM, et al. for the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics – 2012 update. *Circulation*. 2012;125:e2-e220.

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- <sup>7</sup> Kim JH et al. A national survey of societal cost of acute coronary syndrome in South Korea. Poster presented at ISPOR 13th Annual European Congress 2010; November 2010; Prague, Czech Republic.
- <sup>8</sup> Fox KAA, Steg PG, Eagle KA, et al. Decline in rates of death and heart failure in acute coronary syndromes, 1999-2006. *J Am Med Assoc.* 2007;297:1892-1900.
- <sup>9</sup> Chan MY, Mahaffey KW, Sun LJ, et al. Prevalence, predictors, and impact of conservative medical management for patients with non-ST-segment elevation acute coronary syndromes who have angiographically documented significant coronary disease. *J Am Coll Cardiol.* 2008;1:369-378.