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Eisai Co., Ltd.

# POSITIVE TOPLINE RESULTS OBTAINED FROM LARGE-SCALE CARDIOVASCULAR OUTCOMES TRIAL OF ANTI-OBESITY AGENT BELVIQ®

- *BELVIQ did not increase incidence of cardiovascular events in study of 12,000 obese and overweight patients*
- *Reduction in conversion to type 2 diabetes mellitus in patients without diabetes*
- *Improvement in multiple cardiovascular risk factors including blood pressure, lipids, blood glucose and renal function*

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") has announced that it has obtained the topline results of the ongoing Cardiovascular Outcomes Trial ("CAMELLIA-TIMI61") of lorcaserin hydrochloride (generic name, product name in the U.S.: BELVIQ®, "BELVIQ") in 12,000 patients as a post-marketing clinical trial evaluating safety as the primary objective. BELVIQ was approved in the United States in June 2012 by the U.S. Food and Drugs Administration (FDA) as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients*, and was launched in June 2013.

This study was conducted at over 400 sites in eight countries including the United States in collaboration with the Thrombolysis in Myocardial Infarction (TIMI) Study Group, and is the largest cardiovascular outcome trial conducted to date for a weight loss medication. The study assessed the incidence of major adverse cardiovascular events (MACE: defined as cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in overweight and obese adults with existing cardiovascular disease or type 2 diabetes mellitus (T2DM) with cardiovascular risk factors who were administered BELVIQ 10 mg twice-daily.

From the results, CAMELLIA-TIMI 61 met its primary safety objective, finding that long-term treatment with BELVIQ does not increase incidence of MACE. With this result, BELVIQ is the first ever weight loss medication approved for chronic weight management to achieve this safety objective in a dedicated long-term cardiovascular outcome trial.

Since the study met the primary safety endpoint of MACE, the study also assessed whether or not BELVIQ reduced the incidence of MACE+ (consisting of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, hospitalization due to unstable angina, heart failure or coronary revascularization) compared to placebo as the primary efficacy endpoint. Although statistical superiority to placebo was not met, the results successfully confirmed statistical non-inferiority for BELVIQ.

On the other hand, CAMELLIA-TIMI 61 also assessed for effects of BELVIQ on multiple cardiovascular risk factors. On top of standard of care for cardiovascular risk management, treatment with BELVIQ resulted in significant improvements in a number of predefined secondary endpoints, including blood pressure, lipids, blood glucose and renal function, as well as a reduction in conversion to T2DM in patients without diabetes at baseline.

In additional subgroup analyses, on a background of lifestyle modification, it was observed that BELVIQ improved long-term weight loss compared to placebo, including in subpopulations with T2DM and obstructive sleep apnea.

The overall safety profile for BELVIQ in CAMELLIA-TIMI 61 was consistent with that of the approved label. Dizziness, urinary tract infection, and fatigue being the most commonly reported adverse events in CAMELLIA-TIMI 61.

“Obesity is a major problem globally and associated with risk for heart disease and other serious health conditions such as hypertension, type 2 diabetes, and obstructive sleep apnea,” said Lynn Kramer, M.D., Chief Clinical Officer and Chief Medical Officer, Neurology Business Group, Eisai. “The results for BELVIQ from this robust global study provide important information to physicians and patients, particularly those with cardiovascular and obesity-related complications.”

“CAMELLIA-TIMI61 was a rigorous evaluation of the safety and efficacy of BELVIQ as a metabolic intervention on cardiovascular health in a high cardiovascular risk patient population,” said Marc Sabatine, MD, MPH, Chairman, TIMI Study Group, Brigham and Women’s Hospital. “We look forward to sharing the full results with the scientific community.”

Detailed results of the analysis of the study will be presented on August 26 at the European Society of Cardiology Congress 2018 held in Munich, Germany from August 25 to 29, and also on October 4 at the European Association for Study of Diabetes (EASD) Meeting held in Berlin, Germany from October 1 to 5.

With the results of this study, Eisai will have discussions with FDA including potential revision of the product label. By continuing to provide additional clinical and scientific information regarding BELVIQ, Eisai continues to make further contributions to address unmet medical needs and increase the benefits for patients and their families.

* Adult patients with an initial body mass index (BMI) of 30 $kg/m^2$ or greater (obese) or 27 $kg/m^2$ or greater (overweight) in the presence of at least one weight-related comorbid condition

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**[Notes to editors]**

**1. About lorcaserin hydrochloride (U.S. brand name: BELVIQ, once daily formulation U.S. brand name: BELVIQ XR)**

Discovered and developed by Arena Pharmaceuticals, Inc. (Headquarters: California, United States, President and CEO: Amit D. Munshi), lorcaserin is a novel chemical entity that is believed to decrease food consumption and promote satiety by selectively activating serotonin 2C receptors in the brain. Activation of these receptors may help a person eat less and feel full after eating smaller amounts of food. Lorcaserin was approved in June 2012 by the FDA as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of 30 $kg/m^2$ or greater (obese) or 27 $kg/m^2$ or greater (overweight) in the presence of at least one weight-related comorbid condition, and was launched in the United States under the brand name BELVIQ in June 2013 after receiving a final scheduling designation from the U.S. Drug Enforcement Administration (DEA). In addition, lorcaserin has been made available in South Korea via a third-party distributor from 2015. Lorcaserin was approved in Mexico in July 2016 and in Brazil in December 2016, with the same indication as for the United States.

Furthermore, BELVIQ XR, a once-daily formulation of lorcaserin aiming to increase convenience of administration for patients, was approved in the United States in July 2016.

In January 2017, Eisai acquired all of Arena's rights to develop and market BELVIQ.

The most common adverse reactions observed in multiple Phase III clinical studies on lorcaserin were headache, dizziness, fatigue, nausea, dry mouth and constipation in patients without diabetes, and hypoglycemia, headache, back pain, cough and fatigue in patients with diabetes. For further information on lorcaserin in the United States, including Important Safety Information (ISI), please visit the BELVIQ product website (http://www.belviq.com).

**2. About the Cardiovascular Outcomes Trial, CAMELLIA-TIMI61 Study**

The CAMELLIA (Cardiovascular And Metabolic Effects of Lorcaserin In Overweight And Obese Patients) TIMI 61 study is the largest ongoing double-blind, placebo-controlled, parallel-group Phase IIIB/IV study among weight loss medications. The primary safety objective was to evaluate the incidence of major adverse cardiovascular events (MACE), defined as cardiovascular death, myocardial infarction or stroke. If the primary safety objective was met, the efficacy objective was to evaluate the impact of lorcaserin on the incidence of MACE+, defined as MACE or hospitalization due to unstable angina or heart failure, or any coronary revascularization. Secondary objectives included evaluation for the potential to delay or prevent conversion to T2DM in patients with pre-diabetes or no diabetes at baseline and improvement of glycemic control in patients with T2DM.

**3. About the TIMI Study Group**

The TIMI Study Group is an Academic Research Organization based at Brigham and Women’s Hospital that has been leading practice-changing cardiovascular clinical trials for 30 years.