Eisai Inc. Announces Positive Topline Results from CAMELLIA-TIMI61, a Large-Scale Cardiovascular Outcome Trial for the Anti-Obesity Agent BELVIQ

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

WOODCLIFF LAKE, N.J., JULY 17, 2018 – Eisai Inc. announced positive topline results from the CAMELLIA-TIMI 61 cardiovascular outcome trial. This 12,000 patient study of BELVIQ® (lorcaserin HCl) CIV 10 mg twice-daily 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 (CV) outcome trial to date for a weight loss medication. The study was conducted as part of a post-marketing requirement by the US Food and Drug Administration (FDA) with the primary objective to evaluate long-term cardiovascular safety and assessed for the incidence of major adverse cardiovascular events (MACE) in overweight and obese adults with existing cardiovascular disease or type 2 diabetes mellitus (T2DM) with cardiovascular risk factors.

CAMELLIA-TIMI 61 met its primary safety objective, finding that long-term treatment with BELVIQ does not increase incidence of MACE, defined as cardiovascular death or non-fatal myocardial infarction or non-fatal stroke, in overweight and obese patients at high risk for CV events. With this result, BELVIQ is the first- ever weight loss medication approved for chronic weight management to achieve this objective in a dedicated long-term cardiovascular outcome trial.

Since the study met the primary safety endpoint for MACE, the study also assessed for the primary efficacy endpoint of whether or not BELVIQ reduced the incidence of cardiovascular events compared to placebo for a broader composite endpoint, MACE+, consisting of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, hospitalization due to unstable angina, heart failure or coronary revascularization. Although superiority to placebo was not met, BELVIQ was non-inferior to placebo on the MACE+ composite, with similar event rates for BELVIQ and placebo.

CAMELLIA-TIMI 61 also assessed for effects of BELVIQ on multiple cardiovascular risk factors. On top of standard of care for CV risk management, treatment with BELVIQ resulted in significant improvements in a number of predefined secondary endpoints, including blood pressure, lipids, blood sugar 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 of patients 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 increased 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 health care providers 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.”

Eisai and the TIMI Study Group will present results of the CAMELLIA-TIMI 61 study at the European Society for Cardiology (ESC) Meeting in Munich, Germany on August 26 and the European Association for Study of Diabetes (EASD) Meeting in Berlin, Germany on October 4.

With the results of this study, Eisai will have discussions with the US FDA including potential revision of the product label to include meaningful and important information for prescribers. 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.

About BELVIQ®

BELVIQ®/BELVIQ XR® is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults 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 (e.g., hypertension, dyslipidemia, type 2 diabetes).

Limitations of Use:

- The safety and efficacy of co-administration of BELVIQ/BELVIQ XR with other products intended for weight loss, including prescription drugs (e.g., phentermine), over-the-counter drugs, and herbal preparations, have not been established.
- The effect of BELVIQ/BELVIQ XR on cardiovascular morbidity and mortality has not been established.

About the Study

The **CAMELLIA** (**C**ardiovascular **A**nd **M**etabolic **E**ffects of **L**orcaserin **I**n Overweight **A**nd Obese Patients) **TIMI 61** study was the largest double-blind, placebo-controlled, parallel-group Phase IIIB/IV study among weight loss medications. The study consisted of over 12,000 overweight and obese patients with established CV disease or CV risk factors.

The primary safety objective was to evaluate that BELVIQ did not increase the incidence of major adverse cardiovascular events (MACE), defined as cardiovascular death, non-fatal myocardial infarction or non-fatal stroke. If the primary safety objective was met, the efficacy objective was to evaluate the impact of BELVIQ on reducing 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.

Important Safety Information

Contraindications

- Pregnancy: BELVIQ/BELVIQ XR should not be taken during pregnancy or by women who are planning to become pregnant.
- Hypersensitivity: Patients with prior hypersensitivity reactions to lorcaserin or to any of the product components should not take BELVIQ/BELVIQ XR. Hypersensitivity reactions have been reported.

Warnings and Precautions

- **Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions:** BELVIQ/BELVIQ XR is a serotonergic drug. The development of potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported during use of serotonergic drugs, including, but not limited to, selective serotonin-norepinephrine reuptake inhibitors, and selective serotonin reuptake inhibitors, tricyclic antidepressants, bupropion, triptans, dietary supplements such as St. John's Wort and tryptophan, drugs that impair metabolism of serotonin (including monoamine oxidase inhibitors), dextromethorphan, lithium, tramadol, antipsychotics or other dopamine antagonists, particularly when used in combination. Patients should be monitored for the emergence of serotonin syndrome symptoms or NMS-like reactions, including agitation, hallucinations, coma, tachycardia, labile blood pressure, hyperthermia, hyperreflexia, incoordination, nausea, vomiting, diarrhea, and muscle rigidity. Treatment with BELVIQ/BELVIQ XR and any concomitant serotonergic or antidopaminergic agents should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated.
- **Valvular heart disease:** Patients should not take BELVIQ/BELVIQ XR in combination with potent 5-HT_{2B} receptor agonists that have been associated with regurgitant valvular heart disease (e.g., cabergoline). In clinical trials, 2.4% of patients taking BELVIQ and 2.0% of patients taking placebo developed valvular regurgitation: none of these patients were symptomatic. BELVIQ/BELVIQ XR should be used with caution in patients with congestive heart failure (CHF). Patients who develop signs and symptoms of valvular heart disease, including dyspnea, dependent edema, CHF, or a new cardiac murmur, should be evaluated and discontinuation of BELVIQ/BELVIQ XR should be considered.
- **Cognitive impairment:** Impairment in attention, memory, somnolence, confusion, and fatigue have been reported in patients taking BELVIQ. Patients should not drive a car or operate heavy machinery until they know how BELVIQ/BELVIQ XR affects them.
- **Psychiatric disorders:** The recommended daily dose should not be exceeded, as higher doses may cause euphoria, hallucination, and dissociation. Monitor patients for the development or worsening of depression, suicidal thoughts or behaviors, and/or any changes in mood. Discontinue BELVIQ/BELVIQ XR in patients who develop suicidal thoughts or behaviors.
- **Hypoglycemia:** Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus who are being treated with antidiabetic medications, so measurement of blood sugar levels before and during treatment with BELVIQ/BELVIQ XR is recommended. Decreases in doses of antidiabetic medications or changes in medication regimen should be considered.
- **Priapism:** Men who experience priapism should immediately discontinue BELVIQ/BELVIQ XR and seek emergency medical attention. BELVIQ/BELVIQ XR should be used with caution with erectile dysfunction medications. BELVIQ/BELVIQ XR should be used with caution in men who have conditions that might predispose them to priapism (e.g., sickle cell anemia, multiple myeloma, or leukemia), or in men with anatomical deformation of the penis (e.g., angulation, cavernosal fibrosis, or Peyronie's disease).
- **Heart rate decreases:** Because BELVIQ/BELVIQ XR may cause a slow heartbeat, it should be used with caution in patients with a history of bradycardia or heart block greater than first degree.
- **Monitoring Considerations:** Consider monitoring for CBC changes, signs and symptoms of prolactin excess, and pulmonary hypertension.

Most Common Adverse Reactions for BELVIQ

- In patients without diabetes: headache (17%), dizziness (9%), fatigue (7%), nausea (8%), dry mouth (5%), and constipation

(6%).
- In patients with diabetes: hypoglycemia (29%), headache (15%), back pain (12%), cough (8%), and fatigue (7%).

Most Common Adverse Reactions for BELVIQ XR

- Common side effects in patients on BELVIQ XR were similar to those seen in patients on BELVIQ.

Nursing Mothers

- BELVIQ/BELVIQ XR should not be taken by women who are nursing.

BELVIQ/BELVIQ XR is a federally controlled substance (CIV) because it may be abused or lead to dependence.
For more information about BELVIQ/BELVIQ XR, see full Prescribing Information.

About Obesity

Obesity is a serious and growing public health issue. The prevalence of obesity in the U.S. has more than doubled among adults in the past 30 years. Approximately 69 percent of American adults over the age of 20 are affected by obesity and overweight. This dramatic rise in obesity has also had a major impact on other diseases. Indeed, obesity is an important risk factor for heart disease and stroke, directly or indirectly through intervening risk factors, such as hypertension, dyslipidemia, and diabetes.

About Eisai Inc.
At Eisai Inc., *human health care (hhc)* is our goal. We give our first thoughts to patients and their families, and helping to increase the benefits health care provides. As the U.S. pharmaceutical subsidiary of Tokyo-based Eisai Co., Ltd., we have a passionate commitment to patient care that is the driving force behind our efforts to discover and develop innovative therapies to help address unmet medical needs.

Eisai is a fully integrated pharmaceutical business that operates in two global business groups: oncology and neurology (dementia-related diseases and neurodegenerative diseases). Each group functions as an end-to-end global business with discovery, development, manufacturing and marketing capabilities. Our U.S. headquarters, commercial and clinical development organizations are located in New Jersey; our discovery labs are in Massachusetts and Pennsylvania; and our global demand chain organization resides in Maryland and North Carolina. To learn more about Eisai Inc., please visit us at www.eisai.com/US and follow us on Twitter and LinkedIn.

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. Brigham and Women's Hospital (BWH) is a 793-bed nonprofit teaching affiliate of Harvard Medical School and a founding member of Partners HealthCare. BWH has more than 3.5 million annual patient visits, is the largest birthing center in New England and employs nearly 15,000 people.