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Interim Results Presented from Long-Term, Open-Label Extension Study Evaluating Lundbeck's ONFI™ (clobazam) in the Adjunctive Treatment of Drop Seizures Associated with LGS

Study includes adult and pediatric patients (two years of age or older) with a current or previous diagnosis of LGS who have continued to receive ONFI as add-on therapy for as long as two years¹

Savannah, Ga., October 27, 2011 – Today, Lundbeck Inc. presented interim data from its long-term, open-label extension study evaluating ONFI™ (clobazam) CIV for the adjunctive treatment of drop seizures associated with Lennox-Gastaut syndrome (LGS). These interim results support the reductions in drop seizure rates associated with ONFI when used as add-on therapy for adult and pediatric patients, two years of age or older, with a current or previous diagnosis of LGS.¹ Results of this study were presented at the annual meeting of the Child Neurology Society in Savannah, Ga. (Poster No. DD-26). ONFI was approved by the U.S. Food and Drug Administration (FDA) earlier this week for the adjunctive treatment of seizures associated with LGS in patients two years and older.²

LGS is a rare and severe form of epilepsy that is typically diagnosed in childhood and often persists into adulthood.^{3,4,5} LGS is associated with multiple types of seizures with periods of frequent seizures, and daily seizures are common.⁶ Some of these seizures, including atonic, tonic and myoclonic seizures, may cause falls, or “drop seizures” (also referred to as “drop attacks”), which may result in injury.⁷

“This interim analysis showed drop seizure reduction associated with ONFI for the add-on treatment of drop seizures associated with LGS, and supports findings from the pivotal, double-blind Phase III clinical trial evaluating the therapy,” said Yu-Tze Ng, director of epilepsy at the University of Oklahoma College of Medicine and lead investigator in the study. “We look forward to finalizing data from this open-label study to provide physicians with more information about the use of ONFI for patients with a history of LGS who continue to have seizures due to the intractable nature of the disease.”⁸

This multicenter, open-label study enrolled patients with a current or previous diagnosis of LGS aged 2 to 60 years old.¹ Patients had previously completed one of two Lundbeck-sponsored, double-blind clinical trials evaluating ONFI as adjunctive therapy for seizures associated with LGS and were given the option of tapering off ONFI or continuing in this open-label study.¹ Of 306 patients previously enrolled in these two earlier studies, 267 entered the open-label study during the enrollment period of Dec. 28, 2005 through Dec. 15, 2009;¹ this interim analysis includes data collected through July 1, 2010.¹ At the time of this analysis, 213 patients (80%) remained in the study, with 189 having stayed in the study for at least one year and 94 for at least two years.¹

Data from the study's primary efficacy endpoint showed that the median percentage decrease (from baseline period in previous study) in average weekly rate of drop seizures was 71.1 percent at month 3 (N=252) and was sustained through the cut-off date for this interim analysis.¹ At the time of this interim analysis, dosage increases were not needed, which is consistent with findings from the pivotal, double-blind Phase III clinical trial.¹ Dosing was titrated per the individual patient with a maximum dose of 80 mg per day.

The most common adverse events (AEs), defined as greater than or equal to 10 percent, reported were upper respiratory tract infection (25.1%), somnolence (24.3%), pyrexia (18.4%) and pneumonia (15.4%).¹

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About the Study

This multicenter, open-label study of ONFI is designed to assess the long-term safety and efficacy of open-label ONFI as adjunctive therapy for patients with seizures associated with LGS.¹ Qualifying patients from the following Lundbeck-sponsored studies were given the opportunity of continuing in this open-label study.¹

- Dose-Ranging Study (Phase II; N=68): A 7-week randomized, double-blind study consisting of a 4-week baseline period, 3-week blinded titration period and 4-week blinded maintenance period, followed by open-label continuation or 3-week taper period.² Patients in the dose-ranging study received either low-dose (0.25 mg/kg/day; n=32) or high-dose (1.0 mg/kg/day; n=36) regimens of ONFI along with up to three other AEDs.²
- The CONTAIN Trial (Phase III; N=238): A 15-week, randomized, double-blind, placebo-controlled study consisting of a 4-week baseline period, 3-week blinded titration period and 12-week blinded maintenance period, followed by open-label continuation or 3-week taper period.² Patients in the CONTAIN Trial received either placebo or one of three dosages of ONFI: High (1.0 mg/kg/day; n=59), Medium (0.5 mg/kg/day; n=62), Low (0.25 mg/kg/day; n=58).²

Patients were eligible to continue on to the open-label study if no more than 14 days elapsed since their last dose in the dose-ranging study (Phase II) or the CONTAIN Trial.¹ For patients from the CONTAIN Trial, ONFI was started at a target dosage of 0.5 mg/kg/day (maximum 40 mg/day).¹ This dosage was maintained for 48 hours, and thereafter adjusted per clinical need.¹ For patients from the dose-ranging study who chose to continue in the open-label study, the unblinded physician adjusted or maintained the dosage the patient was previously receiving.¹ While target dosages did not exceed 1.0 mg/kg/day (maximum 40 mg/day) in the CONTAIN Trial and the dose-ranging study, a target dosage of 2.0 mg/kg/day (maximum 80 mg/day) was allowed in the open-label extension study.¹

About ONFI™ (clobazam)

ONFI is an oral antiepileptic drug developed in the United States by Lundbeck Inc., and will be available in 5 mg, 10 mg, and 20 mg tablets. ONFI is a 1,5-benzodiazepine. The exact mechanism of action for ONFI is not fully understood, but is thought to involve potentiation of GABAergic neurotransmission resulting from binding at the benzodiazepine site of the GABA_A receptor.¹

ONFI (pronounced "ON-fee") will be available in U.S. pharmacies in early January and is a federally controlled schedule four substance (CIV).

Important Safety Information¹

- ONFI is a prescription medicine used along with other medicines to treat seizures associated with Lennox-Gastaut syndrome in people 2 years of age or older.
- **ONFI can make you sleepy or dizzy and can slow your thinking and make you clumsy which may get better over time.** Do not drive, operate heavy machinery, or other dangerous activities until you know how ONFI affects you. Do not drink alcohol or take other drugs that may make you sleepy or dizzy while taking ONFI without first talking to your healthcare provider as your sleepiness or dizziness may get much worse.
- **ONFI can cause withdrawal symptoms.** Do not stop suddenly taking ONFI without first talking to a healthcare provider. Stopping ONFI suddenly can cause seizures that will not stop (status epilepticus), hearing or seeing things that are not there (hallucinations), shaking, nervousness, and stomach and muscle cramps.
- **ONFI can be abused and cause dependence.** Physical dependence is not the same as drug addiction. Talk to your healthcare provider about the differences. **ONFI is a federally controlled substance (C-IV) because it can be abused or lead to dependence.**
- **Like other antiepileptic drugs, ONFI may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.** Call your healthcare provider right away if you have any symptoms, especially sudden changes in mood, behaviors, thoughts, or feelings, and especially if they are new, worse, or worry you.
- If you are pregnant or plan to become pregnant, ONFI may harm your unborn baby. You and your healthcare provider will have to decide if you should take ONFI while you are pregnant.

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- ONFI can pass into breast milk. You and your healthcare provider should decide if you should take ONFI or breast feed. You should not do both.
- The most common side effects seen in ONFI patients include: sleepiness; drooling; constipation; cough; pain with urination; fever; acting aggressive, being angry or violent; difficulty sleeping; slurred speech; tiredness and problems with breathing.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

For more information, please see the [ONFI Medication Guide](#) and [Full Prescribing Information](#).

About Lundbeck Inc.

Headquartered in Deerfield, Illinois, Lundbeck Inc., a wholly-owned subsidiary of H. Lundbeck A/S, is committed to developing and providing innovative specialty therapies that fulfill unmet medical needs of people with central nervous system (CNS) disorders, including rare diseases. For more information, please visit www.lundbeckinc.com.

About Lundbeck

H. Lundbeck A/S (LUN.CO, LUN DC, HLUKY) is an international pharmaceutical company highly committed to improving the quality of life for people suffering from central nervous system (CNS) disorders. For this purpose, Lundbeck is engaged in the research, development, production, marketing and sale of pharmaceuticals across the world. The company's products are targeted at disorders such as depression and anxiety, schizophrenia, insomnia, epilepsy, Huntington's, Alzheimer's and Parkinson's diseases.

Lundbeck was founded in 1915 by Hans Lundbeck in Copenhagen, Denmark. Today Lundbeck employs approximately 5,900 people worldwide. Lundbeck is one of the world's leading pharmaceutical companies working with CNS disorders. In 2010, the company's revenue was DKK 14.8 billion (approximately EUR 2.0 billion or USD 2.6 billion). For more information, please visit www.lundbeck.com.

ONFI is a trademark of Lundbeck Inc.

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Sources

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