Open-label Continuation Study Supports Long-term Efficacy of Xenazine® (tetrabenazine) for the Treatment of Chorea Associated with Huntington’s Disease

Results achieved over 80 weeks of treatment consistent with statistically significant reduction in chorea demonstrated in pivotal study

DEERFIELD, Ill., March 5, 2010 – Lundbeck Inc. today announced the presentation of results from an open-label extension study of Xenazine® (tetrabenazine) for the treatment of chorea associated with Huntington’s disease (HD). Data from this study demonstrated that after an 80-week treatment period, subjects treated with Xenazine experienced a statistically significant reduction in chorea score (p<0.0001) as measured using the Unified Huntington’s Disease Rating Scale (UHDRS) compared with baseline. These results are consistent with the reduction in chorea score observed in a pivotal Phase 3 randomized, double-blind, placebo-controlled multi-center clinical study in which subjects were treated with Xenazine for 12 weeks. Data from the open-label study will be presented today at the 12th Annual American Society of Experimental NeuroTherapeutics (ASENT) meeting in Bethesda, Maryland (Poster No. 0029). Results of this study are published in BMC Neurology, an online open access journal at http://www.biomedcentral.com/bmcneurol. Xenazine carries a boxed warning for increased risk of depression and suicidality.

“The jerky, sporadic movements commonly seen with chorea associated with Huntington’s disease may make it difficult for affected individuals to do tasks such as holding on to objects or even walking,” said Dr. Samuel Frank, MD, assistant professor of neurology at the Boston University School of Medicine and lead investigator in this study. “Prolonged reduction of chorea associated with HD in some patients, as seen in this open-label study of Xenazine, is highly encouraging and suggests that Xenazine could be an important treatment option for those seeking to lessen chorea.”

This open-label, multi-center extension study was designed to assess the long-term use of Xenazine as a treatment for chorea associated with Huntington’s disease. The study enrolled 75 subjects, all of whom had previously completed 12 weeks of treatment with Xenazine in the pivotal Phase 3 trial, followed by a one week washout period. Xenazine was titrated over a maximum 12 weeks every three to seven days to the best individual dose, up to a maximum of 200 mg/day of Xenazine. Titration was permitted only during the first 11 weeks of the study. Patients who appear to require doses of greater than 50 mg/day should be genotyped for CYP2D6. Doses above 100 mg/day are not recommended for any patient in the Xenazine full prescribing information.

Of the 75 subjects enrolled in the study, 45 subjects completed the 80-week treatment period, of which 42 subjects continued on to complete a one-week washout period. Thirty subjects withdrew from the study, of which, three subjects withdrew due to adverse events associated with Xenazine, including depression, delusions associated - more-
with previous suicidal behavior and vocal tics, and 26 subjects withdrew for various other reasons. One subject died due to metastatic breast cancer.

The primary efficacy endpoint in this study was the Total Maximal Chorea (TMC) score from the UHDRS at week 80 compared with baseline TMC score.\(^1\) TMC score at week 80 was also compared to TMC score at week 81 following the washout period.\(^2\) The UHDRS is a validated rating system used to measure the severity of Huntington's disease.\(^2\) The rating system ranges from 0 units (absent chorea symptoms) to 28 units (marked/prolonged chorea).

Data from this study demonstrate a statistically significant reduction in chorea in patients compared to baseline who completed 80 weeks of Xenazine treatment, with a mean reduction in the TMC score of 4.6 UHDRS units.\(^3\) At week 81, following a one week washout period, the mean TMC score increased 5.3 UHDRS units compared to week 80 (p<0.001), suggesting that continued use of Xenazine at an individualized dose maintains reduction of chorea associated with HD for up to 80 weeks and confirming results from the pivotal study where discontinuation of Xenazine treatment was associated with the return of chorea, but without significant worsening compared to baseline.\(^1\)

When mild and unrelated adverse events (AEs) were excluded, the most common AEs in this study reported in >5% of subjects (three or more) were sedation/somnolence, depressed mood, anxiety, insomnia, akathisia, fatigue, agitation, fall, dysphagia and dystonia.\(^1\) Thirty-nine patients reported at least one AE during the titration phase compared to 20 patients during the maintenance period. Insomnia, somnolence and diarrhea emerged during titration and resolved during the maintenance period. Twelve serious AEs were reported including two falls, two cancer diagnoses, a single suicide attempt, pneumonia, elective hip replacement with post-op agitation, agitation, anxiety, akathisia, and one abnormal CA 27-29 titer in a patient who later died due to metastatic breast cancer.\(^1\)

**About Xenazine**
Xenazine is the only FDA-approved therapy for the treatment of chorea associated with Huntington’s disease. Xenazine was approved by the U.S. Food and Drug Administration (FDA) in August 2008 and was launched by Lundbeck Inc. in November 2008. To learn more about Xenazine, visit [www.xenazineusa.com](http://www.xenazineusa.com).

**Xenazine Important Safety Information and Boxed Warning**
Xenazine can increase the risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington’s disease. Anyone considering the use of Xenazine must balance the risks of depression and suicidality with the clinical need for control of choreiform movements. Close observation of patients for the emergence or worsening of depression, suicidality, or unusual changes in behavior should accompany therapy. Patients, their caregivers, and families should be informed of the risk of depression and suicidality and should be instructed to report behaviors of concern promptly to the treating physician.

Particular caution should be exercised in treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency in Huntington’s disease. Xenazine is contraindicated in patients who are actively suicidal, and in patients with untreated or inadequately treated depression.
Xenazine is also contraindicated in patients with impaired hepatic function, and in patients taking monoamine oxidase inhibitors or reserpine. At least 20 days should elapse after stopping reserpine before starting Xenazine. Although Xenazine has been shown to decrease the chorea associated with HD, it was also shown to cause slight worsening in mood, cognition, rigidity and functional capacity and prescribers should periodically re-evaluate the need for therapy. Some adverse effects such as depression, fatigue, insomnia, sedation/somnolence, parkinsonism, akathisia, QTc prolongation and interactions with CYP2D6 inhibitors may be dose dependent, and resolve or lessen with dose adjustment. The most frequent adverse events (over 10% and at least 5% greater than placebo) reported with Xenazine compared to placebo in a randomized, 12-week, placebo controlled clinical trial of HD subjects include sedation/somnolence (31% vs. 3%), fatigue (22% vs. 13%), insomnia (22% vs. 0%), depression (19% vs. 0%), akathisia (19% vs. 0%), anxiety (15% vs. 3%) and nausea (13% vs. 7%). For more information, please see full prescribing information including Boxed Warning or go to www.xenazineusa.com.

**About Chorea Associated with Huntington’s Disease**
Chorea is the most common symptom of Huntington’s disease (HD), a rare neurodegenerative disease that results in uncontrolled movements, emotional disturbances, and mental deterioration. HD affects approximately 30,000 people in the United States. Chorea associated with HD is characterized by irregular, abrupt movements of the face, fingers, arms, legs, or body that can appear as constant jerky, twisting, and uncontrollable, dance-like motions. As the disease progresses, it may interfere with many voluntary movements, making it more difficult to walk, talk or hold things. Currently, there is no known cure for HD and the disease and prognosis is poor. To learn more about chorea associated with Huntington’s disease, please visit www.xenazineusa.com.

**About Lundbeck Inc.**
Lundbeck Inc., a subsidiary of H. Lundbeck A/S of Copenhagen, Denmark, is a specialty pharmaceutical company with proven success in developing and commercializing high-need treatments. The company is committed to providing innovative therapies that fulfill unmet medical needs of people with CNS disorders and rare diseases for which few, if any, effective treatments are available. For more information, please visit www.lundbeckinc.com.

**About H. Lundbeck A/S**
H. Lundbeck A/S (LUN.CO, LUN DC, HLUKY) is an international pharmaceutical company committed to improve the quality of life for people suffering from CNS disorders. For this reason, Lundbeck is engaged in the research and development, production, marketing and sale of pharmaceuticals across the world, targeted at disorders like depression and anxiety, schizophrenia, insomnia, Huntington’s, Alzheimer’s and Parkinson’s diseases. Lundbeck was founded by Hans Lundbeck in 1915 in Copenhagen, Denmark, and today employs over 5,500 people worldwide. Lundbeck is one of the world’s leading pharmaceutical companies working with CNS disorders. In 2009, the company’s revenue was DKK 13.7 billion (approximately EUR 1.8 billion or USD 2.6 billion). For more information, please visit www.lundbeck.com.

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