Results of a New Study of Brintellix® (vortioxetine) vs. Escitalopram on Sexual Functioning in Well Treated MDD Patients Experiencing Treatment-Emergent Sexual Dysfunction

Takeda and Lundbeck Announce Results at American Society of Clinical Psychopharmacology Annual Meeting

Hollywood, Fla., June 17, 2014 —Takeda Pharmaceutical Company Limited (Takeda) and H. Lundbeck A/S (Lundbeck) today announced that the companies will present results about sexual functioning from a head-to-head study of Brintellix® (vortioxetine) vs. escitalopram in patients with well treated major depressive disorder (MDD) experiencing treatment-emergent sexual dysfunction (TESD). The data, accepted as a late-breaker, will be shared in a poster presentation (#41) today at 11:15 a.m. EDT.

In the study, 447 patients with recent major depressive episodes who had responded to SSRI monotherapy but were experiencing TESD were discontinued on their initial treatment and then randomized to Brintellix 10 mg/day or escitalopram 10 mg/day (10 mg for week one and 20 mg for week two of treatment) for eight weeks. The dose of Brintellix or escitalopram could be adjusted after week two, four, or six, as judged by the investigator. The primary endpoint was change from baseline to week 8 in the Changes in Sexual Functioning Questionnaire Short-Form (CSFQ-14) total score using mixed-effects model repeated measures approach (MMRM).

“In this study, patients who were well treated for MDD but experienced treatment-emergent sexual dysfunction showed significant improvement in sexual function with Brintellix vs. escitalopram,” said Anita H. Clayton, M.D., University of Virginia School of Medicine and study investigator. “It is helpful to have a study specifically looking at this side effect that provides more information on the topic of TESD.”

The results demonstrated that patients treated with Brintellix (n=169) experienced a statistically significant improvement, with a mean treatment difference of 2.2 points (95% CI: 0.48–4.02) in the CSFQ-14 total score after eight weeks of treatment (P=0.013; MMRM) compared to escitalopram (n=179). The CSFQ-14 is a clinical and research instrument identifying five scales of sexual functioning and yields scores for three scales corresponding to the phases of the sexual response cycle.1 Numerically more Brintellix-treated patients were responders (change from baseline in CSFQ-14 total score >3; OR=1.51; P=0.06), as compared with escitalopram. Numerically similar responses on the Montgomery-Åsberg Depression Rating Scale (MADRS) total score were observed between the two groups at the end of week eight. In this study, common adverse events for Brintellix were nausea, headache, and dizziness.

These findings build on the global clinical trial program for Brintellix. The comprehensive clinical trial program evaluating the safety and efficacy of Brintellix was comprised of seven positive pivotal studies, including six 6-8 week short-term studies and one 24-64 week long-term maintenance study that demonstrated statistically significant improvements in overall symptoms of depression in adults with MDD.

The FDA approved Brintellix on September 30, 2013 for the treatment of MDD in adults.

Patients can visit www.brintellix.com to sign up for additional information about this new treatment option.

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About Brintellix (vortioxetine)
The mechanism of the antidepressant effect of Brintellix is not fully understood. It is an inhibitor of serotonin (5-HT) reuptake and that is thought to be a mechanism of its action. It is also an agonist at 5-HT1A receptors, a partial agonist at 5-HT1B receptors and an antagonist at 5-HT3, 5-HT1D and 5-HT7 receptors. The contribution of each of these activities to Brintellix’s antidepressant effect has not been established. It is considered to be the first and only compound with this combination of pharmacodynamic activity. The clinical relevance of this is unknown.

Brintellix was discovered by Lundbeck researchers in Copenhagen, Denmark. The clinical trial program in the U.S. was conducted jointly by Lundbeck and Takeda, and Takeda holds the new drug application for the U.S. market. Brintellix is a trademark of H. Lundbeck A/S and is used under license by Takeda Pharmaceuticals America, Inc.

The World Health Organization has issued an Anatomical Therapeutic Chemical (ATC) code for Brintellix that places it in the category of “Other” antidepressants.

The most commonly observed adverse events in MDD patients treated with Brintellix in 6-8 week placebo-controlled studies (incidence greater than or equal to 5 percent and at least twice the rate of placebo) were nausea, constipation and vomiting. Overall, 5 to 8 percent of the patients who received Brintellix 5 to 20 mg/day in short-term trials discontinued treatment due to an adverse reaction, the most common being nausea, compared with 4 percent of placebo-treated patients in these studies. Brintellix and other antidepressants may cause serious side effects. See Important Safety Information below.

In clinical studies, Brintellix had no significant effect on body weight as measured by the mean change from baseline in 6-8 week placebo-controlled studies. In the 6-month, double-blind, placebo-controlled phase of a long-term study in patients who had responded to Brintellix during the initial 12-week, open-label phase, there was no significant effect on body weight between Brintellix and placebo-treated patients. Brintellix has not been associated with any clinically significant effects on vital signs, including systolic and diastolic blood pressure and heart rate, as measured in placebo-controlled studies.

The recommended starting dose of Brintellix is 10 mg once daily without regard to meals. The dose should then be increased to 20 mg/day, as tolerated, because higher doses demonstrated better treatment effects in trials conducted in the U.S. A dose decrease down to 5 mg/day may be considered for patients who do not tolerate higher doses. The available doses provide important flexibility for physicians to help address the variability of patient needs.

Brintellix is available as 5 mg, 10 mg and 20 mg tablets.

IMPORTANT SAFETY INFORMATION

Suicidal Thoughts or Actions
Antidepressants may increase suicidal thoughts or actions in some children, teens or young adults within the first few months of treatment or when the dose is changed. Depression or other serious mental illnesses are the most important causes of suicidal thoughts or actions. People who have (or have a family history of) bipolar illness, or suicidal thoughts or actions may have a particularly high risk. Pay close attention to any changes, especially sudden changes in mood, behavior, thoughts or feelings. Call your healthcare provider right away if symptoms such as anxiety, irritability, impulsivity, trouble sleeping, aggressive behavior or suicidal thoughts are new, worse or worry you. BRINTELLIX has not been evaluated for use in patients under 18.

Do not take BRINTELLIX if you:

- Are allergic to vortioxetine or any of the ingredients in BRINTELLIX
Please see full www.fda.gov/medwatch

Talk to your healthcare provider.

BRINTELLIX may cause serious side effects including:
Serotonin Syndrome: A potentially life-threatening problem that can happen when medicines such as BRINTELLIX are taken with certain other medicines. Symptoms may include agitation, hallucinations, coma or other changes in mental status; problems controlling movements or muscle twitches, stiffness or tightness; fast heartbeat, high or low blood pressure; sweating or fever; nausea, vomiting or diarrhea.

Abnormal bleeding or bruising: BRINTELLIX and other serotonergic antidepressant medicines may increase your risk of bleeding or bruising, especially if you take the blood thinner warfarin (Coumadin®, Jantoven®), a non-steroidal anti-inflammatory drug (NSAID), or aspirin.

Manic episode: Symptoms may include greatly increased energy; severe trouble sleeping; racing thoughts; reckless behavior; unusually grand ideas; excessive happiness or irritability; talking more or faster than usual.

Low salt (sodium) levels in the blood: Symptoms may include headache; difficulty concentrating, memory changes or confusion; weakness and unsteadiness on your feet; and in severe or sudden cases hallucinations, fainting, seizures or coma. If not treated, severe low sodium levels can cause death.

Before starting BRINTELLIX, tell your healthcare provider if you have or had liver problems, seizures or convulsions, bipolar disorder (manic depression) or mania, low salt (sodium) levels in your blood, bleeding problems, drink alcohol, have any other medical conditions or if you are pregnant, nursing, plan to become pregnant, or plan to nurse.

BRINTELLIX and some medicines may interact with each other, may not work as well, or may cause serious side effects when taken together. Tell your healthcare provider if you plan on or are taking any other prescription and non-prescription medicines, vitamins and herbal supplements including medicines for migraine headaches, such as triptans; medicines used to treat mood, anxiety, psychotic or thought disorders such as tricyclics, lithium, SSRIs, SNRIs, bupropion, buspirone or antipsychotics; MAOIs including linezolid (a specific antibiotic); over-the-counter supplements such as tryptophan or St. John’s wort; and the following medicines: aspirin, NSAIDs, warfarin (Coumadin®, Jantoven®), diuretics, rifampicin, carbamazepine, phenytoin, quinidine, tramadol or fentanyl.

Common side effects of BRINTELLIX include: nausea, constipation or vomiting. These are not all the possible side effects of BRINTELLIX.

Do not start or stop taking BRINTELLIX without talking to your healthcare provider first. Suddenly stopping BRINTELLIX when you take higher doses may cause you to have side effects including headache, stiff muscles, mood swings, sudden outbursts or anger, dizziness or feeling lightheaded, or runny nose.

Until you know how BRINTELLIX affects you, do not drive, operate heavy machinery or engage in other dangerous activities.

Avoid drinking alcohol while taking BRINTELLIX.

Talk to your healthcare provider.
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.

Please see full Prescribing Information and Medication Guide for BRINTELLIX.
The Science of Major Depression
The monoamine-deficiency theory posits that the underlying pathophysiological basis of depression is a depletion of serotonin, norepinephrine or dopamine in the central nervous system. The exact cause of MDD is unknown. Research suggests that there are multiple serotonin receptors that may be important in MDD and may influence many biologic and neurologic processes. The release of bio-chemicals, such as serotonin, dopamine and norepinephrine enables impulses to be passed from one cell to another in the nervous system.

Takeda and Lundbeck Alliance
In September 2007, Lundbeck and Takeda Pharmaceutical Company Limited formed a strategic alliance for the exclusive co-development and co-commercialization in the U.S. and Japan of several compounds in Lundbeck’s pipeline for the treatment of mood and anxiety disorders. The companies co-promote Brintellix in the U.S. The Lundbeck–Takeda alliance in the U.S. benefits from the synergy of Lundbeck’s longstanding expertise and knowledge of psychiatry and Takeda’s understanding and established presence in the very important primary care environment.

About Patient Assistance
Healthcare providers and patients may call 1-800-830-9159 to learn more or obtain application forms for the Help at Hand program, a Patient Assistance Program to help qualified patients who may benefit from Brintellix gain access to this therapy without financial barriers.

About Lundbeck
H. Lundbeck A/S (LUN.CO, LUN DC, HLUYY) is a global pharmaceutical company specialized in brain diseases. For more than 50 years, we have been at the forefront of research within neuroscience. Our development and distribution of pioneering treatments continues to make a difference to people living with brain diseases. Our key areas of focus are alcohol dependence, Alzheimer’s disease, depression/anxiety, epilepsy, Huntington’s disease, Parkinson’s disease, schizophrenia and stroke. Lundbeck’s U.S. business is based in Deerfield, Illinois. To learn more about Lundbeck in the U.S., visit www.lundbeckus.com.

Our approximately 6,000 employees in 57 countries are engaged in the entire value chain throughout research, development, production, marketing and sales, and are committed to improving the quality of life of people living with brain diseases. Our pipeline consists of several late-stage development programs and our products are available in more than 100 countries. We have research centers in China, Denmark and the United States, and production facilities in China, Denmark, France, Italy and Mexico. Lundbeck generated revenue of approximately DKK15 billion in 2012 (EUR 2 billion; USD 2.7 billion).

Lundbeck’s shares are listed on the stock exchange in Copenhagen under the symbol “LUN.” Lundbeck has a sponsored Level 1 ADR program listed in the US (OTC) under the symbol “HLUYY.” For additional information, we encourage you to visit our corporate site www.lundbeck.com.

About Takeda Pharmaceutical Company Limited
Located in Osaka, Japan, Takeda is a research-based global company with its main focus on pharmaceuticals. As the largest pharmaceutical company in Japan and one of the global leaders of the industry, Takeda is committed to strive towards better health for patients worldwide through leading innovation in medicine. Additional information about Takeda is available through its corporate website, www.takeda.com.

About Takeda Pharmaceuticals U.S.A., Inc. and Takeda Development Center Americas, Inc.
Based in Deerfield, Ill., Takeda Pharmaceuticals U.S.A., Inc. and Takeda Development Center Americas, Inc. are subsidiaries of Takeda Pharmaceutical Company Limited, the largest pharmaceutical company in
Japan. The respective companies currently market oral diabetes, CNS, rheumatology, gastroenterology and cardiovascular disease treatments and seek to bring innovative products to people through a pipeline that includes compounds in development for diabetes, gastroenterology, neurology and other conditions. To learn more about these Takeda companies, visit www.takeda.us.

This press release contains forward-looking statements. Forward-looking statements include statements regarding Takeda’s plans, outlook, strategies, results for the future, and other statements that are not descriptions of historical facts. Forward-looking statements may be identified by the use of forward-looking words such as "may," "believe," "will," "expect," "project," "estimate," "should," "anticipate," "plan," "assume," "continue," "seek," "pro forma," "potential," "target," "forecast," "guidance," "outlook" or "intend" or other similar words or expressions of the negative thereof. Forward-looking statements are based on estimates and assumptions made by management that are believed to be reasonable, though they are inherently uncertain and difficult to predict. Investors are cautioned not to unduly rely on such forward-looking statements.

Forward-looking statements involve risks and uncertainties that could cause actual results or experience to differ materially from that expressed or implied by the forward-looking statements. Some of these risks and uncertainties include, but are not limited to, (1) the economic circumstances surrounding Takeda’s business, including general economic conditions in Japan, the United States and worldwide; (2) competitive pressures and developments; (3) applicable laws and regulations; (4) the success or failure of product development programs; (5) actions of regulatory authorities and the timing thereof; (6) changes in exchange rates; (7) claims or concerns regarding the safety or efficacy of marketed products or product candidates in development; and (8) integration activities with acquired companies.

The forward-looking statements contained in this press release speak only as of the date of this press release, and Takeda undertakes no obligation to revise or update any forward-looking statements to reflect new information, future events or circumstances after the date of the forward-looking statement. If Takeda does update or correct one or more of these statements, investors and others should not conclude that Takeda will make additional updates or corrections.

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