



Corporate Release

Lundbeck announces positive results for Brintellix™ (vortioxetine) in adult patients with major depression and inadequate response to SSRI or SNRI therapy

- *In a double-blind comparative study vs agomelatine, Brintellix met primary and secondary endpoints for efficacy and overall functioning in patients with major depression and inadequate response to SSRI/SNRI treatment; vortioxetine was well tolerated*
- *Vortioxetine (10-20 mg/day) showed significant efficacy benefits over agomelatine (25-50 mg/day) with statistically significant differences seen from week 4*
- *Patients with inadequate response to SSRI/SNRI treatment represent a large and important population, for which therapies with novel, multimodal modes of action may provide clinical benefits*

Valby, Denmark, 8 April 2013 - H. Lundbeck A/S (Lundbeck) today announced positive results for the REVIVE study, a double-blind randomized study of Brintellix™ (vortioxetine) versus agomelatine in adults with major depression (MDD) who changed antidepressant treatment after an inadequate response to SSRI or SNRI treatment. In this study, the objective was to compare the efficacy and tolerability of flexible dose treatment with Brintellix (10-20mg/day) versus agomelatine (25-50 mg/day) in this challenging MDD patient population. The study was conducted in Europe and one of the newest antidepressants agomelatine was chosen as a comparator because of its different mode of action from conventional SSRI/SNRI therapies.

Few randomized, double-blind studies comparing treatment strategies in MDD patients who were unresponsive to first-line antidepressant treatment have been conducted. This is one of these few studies which also shows a significant difference between treatments.

*"Patients with inadequate response to current SSRI or SNRI therapies represent a large proportion of patients suffering from major depression. Only a few years ago, the landmark STAR*D study¹ confirmed a significant unmet medical need as only half of patients responded to their first-line treatment, which was an SSRI. First-line treatments in clinical practice are typically SSRIs or SNRIs,"* says Executive Vice President Anders Gersel Pedersen, Head of Research & Development at Lundbeck.

In the REVIVE study, the primary efficacy endpoint was change from baseline to week 8 in MADRS total score. Secondary endpoints included assessments of anxiety symptoms (HAM-A), global clinical judgment (CGI-S, CGI-I) and overall functioning (SDS). Patients were randomized to Brintellix (10-20 mg/day) or agomelatine (25-50 mg/day) for 12 week of double-blind treatment.

On the primary efficacy endpoint, Brintellix (n=252) was statistically significantly superior to agomelatine (n=241) ($p < 0.05$) by 2.2 MADRS points. Significant differences in favor of Brintellix were also found for MADRS, HAM-A, CGI-S, CGI-I and SDS from week 4 onwards ($p < 0.05$). Brintellix was well tolerated, with fewer patient withdrawals in the Brintellix group (5.9%) vs. agomelatine (9.5%). Adverse events were consistent with results from previous clinical phase III studies and included nausea (Brintellix 16% and agomelatine 9%) (incidence $> 5\%$ and higher than agomelatine). Overall, this study confirms that Brintellix is efficacious and well tolerated.

Separately, Lundbeck plans to present further efficacy and safety data from its pivotal clinical programme at the 166th American Psychiatric Association (APA) Annual Meeting in San Francisco, USA, 18-22 May 2013.

About Brintellix (vortioxetine)

Brintellix is under investigation as a multimodal antidepressant that is thought to work through a combination of two complementary mechanisms of action: receptor activity modulation and reuptake inhibition. In vitro studies indicate that Brintellix is a 5-HT_{3,5}-HT₇ and 5-HT_{1D} receptor antagonist, 5-HT_{1B} receptor partial agonist, 5-HT_{1A} receptor agonist and inhibitor of the serotonin transporter (SERT). In vivo non-clinical studies have demonstrated that Brintellix modulates neuronal firing and neurotransmitter release in multiple systems, resulting in enhanced levels of serotonin, noradrenaline, dopamine, acetylcholine and histamine in specific areas of the brain.

The multimodal activity profile of Brintellix is different from the profile of currently anti-depressive medicines.

In 2012, Lundbeck filed Brintellix (formerly described as Lu AA21004) for regulatory approval for the indication of MDD in the EU, Canada and other markets, as well as in the US with its co-development partner, Takeda.

About major depressive disorder (MDD)

Major depressive disorder (MDD) - commonly referred to as major depression — is a highly prevalent, serious and debilitating medical condition. The disease can be described as a complex syndrome of emotional, cognitive and somatic symptoms.

The significant clinical heterogeneity of the disease is frequently cited as a reason for the limited efficacy of currently available antidepressants. While several treatments are available, around 50% of patients remain symptomatic following first-line treatment, and a third fail to achieve full resolution of depressive symptoms after four established treatments¹.

The tolerability of antidepressants and patients' concerns about side effects negatively affect patient outcomes. Patients with MDD who experience at least one severe side effect are twice as likely to discontinue treatment prematurely. Common reasons for premature treatment discontinuation include weight gain, and gastrointestinal and sexual side effects.

MDD is the leading worldwide cause of years lost due to disability, and projected to be the biggest contributor to the worldwide burden of disease by 2030. It is estimated that between a quarter and a



third of the population will develop at least one episode of major depression during their life-time and of these as many as two thirds will have recurrent episodes, and one third will develop a chronic condition.

Depression is associated with significant functional impairment and reduced quality of life. Many patients experience a range of symptoms of the disease that include cognitive symptoms such as difficulty concentrating, forgetfulness and inability to make decisions. Persistence of cognitive symptoms in patients with MDD can contribute to impaired work function and predict poor occupational outcome. Additional treatment strategies are needed to prevent and treat these common and debilitating symptoms of depression.

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About Lundbeck

Lundbeck is a global pharmaceutical company highly committed to improving the quality of life of people living with brain diseases. For this purpose, Lundbeck is engaged in the entire value chain throughout research, development, production, marketing and sales of pharmaceuticals across the world. The company's products are targeted at disorders such as depression and anxiety, psychotic disorders, epilepsy, Huntington's, Alzheimer's and Parkinson's diseases. Lundbeck's pipeline consists of several mid- to late- stage development programs.

Lundbeck employs more than 5,800 people worldwide, 2,000 of whom are based in Denmark. We have employees in 57 countries, and our products are registered in more than 100 countries. We have research centers in Denmark, China and the United States and production facilities in Italy, France, Mexico, China and Denmark. Lundbeck generated revenue of approximately DKK 15 billion in 2012. Lundbeck's shares are listed on the stock exchange in Copenhagen under the symbol "LUN". Lundbeck has a sponsored Level 1 ADR programme listed in the US (OTC) under the symbol "HLUY". For additional information, we encourage you to visit our corporate site www.lundbeck.com.

Safe Harbor/Forward-Looking Statements

The above information contains forward-looking statements that provide our expectations or forecasts of future events such as new product introductions, product approvals and financial performance.

Such forward-looking statements are subject to risks, uncertainties and inaccurate assumptions. This may cause actual results to differ materially from expectations and it may cause any or all of our forward-looking statements here or in other publications to be wrong. Factors that may affect future results include interest rate and currency exchange rate fluctuations, delay or failure of development projects, production problems,



unexpected contract breaches or terminations, government-mandated or market-driven price decreases for Lundbeck's products, introduction of competing products, Lundbeck's ability to successfully market both new and existing products, exposure to product liability and other lawsuits, changes in reimbursement rules and governmental laws and related interpretation thereof, and unexpected growth in costs and expenses.

Certain assumptions made by Lundbeck are required by Danish Securities Law for full disclosure of material corporate information. Some assumptions, including assumptions relating to sales associated with product that is prescribed for unapproved uses, are made taking into account past performances of other similar drugs for similar disease states or past performance of the same drug in other regions where the product is currently marketed. It is important to note that although physicians may, as part of their freedom to practice medicine in the US, prescribe approved drugs for any use they deem appropriate, including unapproved uses, at Lundbeck, promotion of unapproved uses is strictly prohibited.

¹ Rush et al; Am J Psych 2006; 163: 1905-1917