**H. Lundbeck A/S**

Ottiliavej 9 Tel +45 36 30 13 11 E-mail investor@lundbeck.com
DK-2500 Valby, Copenhagen www.lundbeck.com
CVR number: 56759913
LEI code: 5493006R4KC2OI5D3470

Corporate Release

# Lundbeck and Takeda receive Complete Response Letter from the FDA for Trintellix® (vortioxetine) sNDA

**Valby, Denmark and Osaka, Japan, 23 June 2017** - H. Lundbeck A/S (Lundbeck) and Takeda Pharmaceutical Company Limited (Takeda) today announced that after providing additional analysis, the U.S. Food and Drug Administration (FDA) has issued a Complete Response Letter (CRL) regarding the supplemental new drug application (sNDA) to include new data in the clinical trials section of the U.S. prescribing information of Trintellix (vortioxetine) for treating aspects of cognitive dysfunction in adults with major depressive disorder (MDD).

Takeda and Lundbeck are disappointed, but we believe in the strength of the data and plan to continue discussions with the FDA on potential paths forward. The companies remain committed to the depression community and Trintellix as a treatment option for adult patients living with depression, including those who suffer from cognitive dysfunction as part of this disease.

The FDA approved Trintellix on 30 September 2013 for the treatment of MDD in adults. The CRL does not change the FDA-approved current prescribing information for Trintellix.

## About Trintellix (vortioxetine)

The mechanism of the antidepressant effect of Trintellix 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-$HT_{1A}$ receptors, a partial agonist at 5-$HT_{1B}$ receptors and an antagonist at 5-$HT_3$, 5-$HT_{1D}$ and 5-$HT_7$ receptors. The contribution of each of these activities to Trintellix'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.

Trintellix 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. Trintellix 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 Trintellix that places it in the category of "Other" antidepressants.

The most commonly observed adverse events in MDD patients treated with Trintellix in 6-8 week placebo-controlled studies (incidence greater than or equal to 5% and at least twice the rate of placebo) were nausea, constipation and vomiting. Overall, 5% to 8% of the patients who received Trintellix 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. Trintellix and other antidepressants may cause serious side effects.

In clinical studies, Trintellix 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 Trintellix during the initial 12-week, open-label phase, there was no significant effect on body weight between Trintellix and placebo-treated patients. Some reports of weight gain have been received since product approval. Trintellix 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.

In the U.S., the recommended starting dose of Trintellix 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.

Trintellix is available as 5 mg, 10 mg and 20 mg tablets in the U.S.

## Lundbeck contacts


Investors:

Palle Holm Olesen
Vice President, Investor Relations
PALO@lundbeck.com
+45 30 83 24 26

Media:

Mads Kronborg
Senior Director, Corp. Communication
MAVK@lundbeck.com
+45 36 43 40 00


## Takeda Pharmaceutical Company Limited Contacts


Japanese media
Tsuyoshi Tada
Tel: +81 (0) 3-3278-2417
Email: tsuyoshi.tada@takeda.com

Media outside Japan
Roseanne Durril
Tel: +1-224-554-1474
Email: roseanne.durril@takeda.com


## About H. Lundbeck A/S

H. Lundbeck A/S (LUN.CO, LUN DC, HLUYY) is a global pharmaceutical company specialized in psychiatric and neurological disorders. For more than 70 years, we have been at the forefront of research within neuroscience. Our key areas of focus are Alzheimer's disease, depression, Parkinson's disease and schizophrenia.

Our approximately 5,000 employees in 55 countries are engaged in the entire value chain throughout research, development, manufacturing, marketing and sales. Our pipeline consists of several late-stage development programmes and our products are available in more than 100 countries. We have production facilities in Denmark, France and Italy. Lundbeck generated revenue of DKK 15.6 billion in 2016 (EUR 2.1 billion; USD 2.2 billion).

For additional information, we encourage you to visit our corporate site www.lundbeck.com and connect with us on Twitter at @Lundbeck.

## About Takeda Pharmaceutical Company

Takeda Pharmaceutical Company Limited is a global, research and development-driven pharmaceutical company committed to bringing better health and a brighter future to patients by translating science into life-changing medicines. Takeda focuses its R&D efforts on oncology, gastroenterology and central nervous system therapeutic areas plus vaccines. Takeda conducts R&D both internally and with partners to stay at the leading edge of innovation. New innovative products, especially in oncology and gastroenterology, as well as Takeda's presence in Emerging Markets, are currently fuelling the growth of Takeda. More than 30,000 Takeda employees are committed to improving quality of life for patients, working with Takeda's partners in health care in more than 70 countries. For more information, visit http://www.takeda.com/news/.

### 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.**