Press release

Valby, Denmark and Otsaka, Japan 20 September 2019

Lundbeck and Takeda announce Ministry of Health, Labour and Welfare (MHLW) approval of Trintellix® in Japan

- **New treatment option with a new pharmacological profile for adult patients with Major Depressive Disorder (MDD) and depressed state in Japan**
- **Phase III clinical trial in Japan with 493 adults with major depressive disorder show that the vortioxetine groups demonstrated statistically significant antidepressant efficacy compared to the placebo group**
- **There are approximately three million patients with the disease in Japan, affecting 2.5% of the population***

H. Lundbeck A/S (Lundbeck) and Takeda Pharmaceutical Company Limited (TSE: 4502/NYSE: TAK) (Takeda) jointly announced today that the MHLW of Japan approved Trintellix® (vortioxetine) for the treatment of depression and depressed state.

The NDA filing submitted to the MHLW in September 2018 included data from a pivotal phase III trial (NCT02389816), which demonstrated statistically significant improvement in overall symptoms of depression in adults as compared to placebo. The regulatory submission also featured data from three other pivotal studies conducted globally (NCT01255787) and in Japan (NCT01355081, NCT01395147).

This study was conducted as a randomized, placebo-controlled, double-blind, parallel-group trial in 493 adult patients in Japan with recurrent depression. Patients were randomly assigned to a vortioxetine 10mg, 20mg or placebo group. The primary endpoint was change in total score from baseline (at the onset of double blinding) on the Montgomery-Åsberg Depression Rating Scale (MADRS) to week 8 of administration compared to placebo. The study demonstrated positive results of vortioxetine including the primary endpoint as compared to placebo for the treatment of MDD in adults.

“MDD remains a serious and complicated disease and I firmly believe that Trintellix will be an important new treatment option for patients in Japan, and health care professionals”, said Naoyoshi Hirota, head of Takeda Development Center Japan.

“I am pleased that individuals suffering from depression in Japan now also have access to this new treatment option. Today’s approval of Trintellix, furthermore, represents a new chapter in Lundbeck’s commercial expansion as we will have our own commercial organization behind the launch of Trintellix in Japan in collaboration with our partner Takeda“, said Jacob Tolstrup, Executive Vice President, Commercial Operations at Lundbeck.

In 2007 Lundbeck formed an agreement with Takeda on the co-development and potential co-commercialization in Japan of Lundbeck's vortioxetine. As communicated in September 2018, Takeda and Lundbeck will co-commercialize Trintellix® in Japan following this approval.

About Major Depressive Disorder (MDD)
MDD is a complex mental health illness that affects approximately 160 million people globally*. MDD is the leading cause of disability worldwide and a major contributor to the overall global burden of disease. MDD may trigger emotional, cognitive and physical symptoms, which include depressed mood, loss of interest or pleasure, significant weight loss or gain or change in appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive guilt, diminished ability to think or concentrate, or indecisiveness, and recurrent suicidal ideation.

About vortioxetine
Vortioxetine has functions of an inhibitor of serotonin reuptake and a regulatory action on serotonin receptors (an antagonist at serotonin3, 7, and 1D receptors, a partial agonist at serotonin 1B receptors and an agonist at serotonin 1A receptors). It is believed to regulate neurotransmission through several systems including the serotonin, norepinephrine, dopamine, acetylcholine and histamine. It is considered to be the first and only compound with this combination of pharmacological activity.

Vortioxetine was invented by Lundbeck researchers in Copenhagen, Denmark. Takeda collaborating with Lundbeck has conducted clinical trials with vortioxetine in Japan.

The U.S Food and Drug Administration (FDA) approved vortioxetine (Trintellix®) on 30 September 2013 for the treatment of MDD in adults. Vortioxetine is furthermore approved in 83 countries (including Europe, Canada, Chile, China, Mexico, Argentina, South Korea, Turkey, Australia, Hong Kong, Singapore and South Africa). Outside North America, vortioxetine is sold as Brintellix®.

An overview of Trintellix® in Japan

Product name	Trintellix® Tablet 10mg, 20mg
Generic name	Vortioxetine hydrobromide
Effects / Indications	Depression and depressed state
Dosage / Administration	Usually for adults, orally take 10mg of Vortioxetine once per day. Depending on the clinical response of the patients, dose can be adjusted up to 20mg per day. The dose should be increased at least 1 week apart.

Disclaimer

The drug information contained herein is intended for the disclosure of Takeda corporate information and is not intended to advertise or promote any prescription drug, including those under development.

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About H. Lundbeck A/S

H. Lundbeck A/S (LUN.CO, LUN DC, HLUYY) is a global pharmaceutical company specialized in brain diseases. For more than 70 years, we have been at the forefront of neuroscience research. We are tirelessly dedicated to restoring brain health, so every person can be their best.

An estimated 700 million people worldwide are living with brain diseases and far too many suffer due to inadequate treatment, discrimination, a reduced number of working days, early retirement and other unnecessary consequences. Every day, we strive for improved treatment and a better life for people living with brain diseases – we call this Progress in Mind.

Read more at www.lundbeck.com/global/about-us/progress-in-mind.

Our approximately 5,500 employees in more than 50 countries are engaged in the entire value chain throughout research, development, production, marketing and sales. Our pipeline consists of several R&D programs and our products are available in more than 100 countries. We have research centres in Denmark and California and our production facilities are located in Denmark, France and Italy. Lundbeck generated revenue of DKK 18,1 billion in 2018 (EUR 2,4 billion; USD 2,8 billion).

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

About Takeda Pharmaceutical Company Limited

Takeda Pharmaceutical Company Limited (TSE:4502/NYSE:TAK) is a global, values-based, R&D-driven biopharmaceutical leader headquartered in Japan, committed to bringing Better

Health and a Brighter Future to patients by translating science into highly-innovative medicines. Takeda focuses its R&D efforts on four therapeutic areas: Oncology, Gastroenterology (GI), Rare Diseases and Neuroscience. We also make targeted R&D investments in Plasma-Derived Therapies and Vaccines. We are focusing on developing highly innovative medicines that contribute to making a difference in people's lives by advancing the frontier of new treatment options and leveraging our enhanced collaborative R&D engine and capabilities to create a robust, modality-diverse pipeline. Our employees are committed to improving quality of life for patients and to working with our partners in health care in approximately 80 countries and regions.
For more information, visit https://www.takeda.com.

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*Source: Global Burden of Disease Study 2017; http://ghdx.healthdata.org/gbd-results-tool
Accessed on September 11, 2019