



## H. Lundbeck A/S

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## Corporate Release

### **Lundbeck and Otsuka report positive phase II data for the combination treatment of brexpiprazole and sertraline for the treatment of Post-Traumatic Stress Disorder (PTSD)**

- *The combination treatment arm of brexpiprazole and sertraline demonstrated improvement in symptoms of PTSD versus placebo ( $p < 0.01$ ) on the primary efficacy endpoint*
- *The efficacy of the combination arm over placebo was also supported by data from multiple secondary endpoints*
- *The companies will discuss the results with the FDA at an end-of-phase-II meeting in 2019*

**Valby, Denmark and Tokyo, Japan, 30 November 2018** - H. Lundbeck A/S (Lundbeck) and Otsuka Pharmaceutical Co., Ltd. (Otsuka) announced today the achievement of positive clinical results (in intention-to-treat population) as measured by the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) total score change from baseline compared to placebo, when brexpiprazole and sertraline was given as combination treatment ( $p < 0.01$ ).

The treatment effects of brexpiprazole alone did not demonstrate clinically meaningful differences in comparison to placebo on the primary endpoint ( $p > 0.35$ ). The treatment effects of sertraline alone also did not demonstrate clinically meaningful differences in comparison to placebo on the primary endpoint ( $p > 0.60$ ).

The randomized, double-blind, placebo-and active-controlled phase II trial was initiated in 2017 and was designed to assess the efficacy, safety and tolerability of flexible doses of brexpiprazole as monotherapy, flexible doses of sertraline as monotherapy or as combination therapy with both brexpiprazole and sertraline in adult subjects with PTSD. The study consisted of a 12-week, double-blind treatment period, including a 1-week placebo run-in period, and a 14-day follow-up after the last dose. A total of 321 participants were randomized to treatment in the study.



The overall safety and tolerability of brexpiprazole were good (and comparable to previous data), when administered as either a combination of brexpiprazole and sertraline or brexpiprazole alone. One (1) incident of death was reported in the placebo group.

The companies plan to meet with the U.S. Food and Drug Administration (FDA) to discuss the results of the phase II study and to evaluate the continuation of a trial programme.

### About PTSD

PTSD is a psychiatric disorder that can develop as a response to traumatic events, such as interpersonal violence, combat, life-threatening accidents or natural disasters. Core features of PTSD include a variety of symptoms, such as re-experiencing phenomena (i.e. flashbacks and nightmares), avoidance behavior, numbing (i.e. amnesia, anhedonia, withdrawal, negativism) and increased arousal (i.e. insomnia, irritability, poor concentration, hypervigilance<sup>1</sup>). Psychiatric co-morbidities are common, and PTSD sufferers can also present with substance abuse, mood and other anxiety disorders, impulsive and dangerous behavior and self-harm.

Across different populations and countries, differences in PTSD prevalence (0.2-4%) can be attributed to geographically specific distributions of trauma type and severity, as well as cross-national and cultural differences in reporting or experiencing PTSD symptoms.

### About brexpiprazole

Brexpiprazole was approved by the U.S. Food and Drug Administration in July 2015 to treat patients with schizophrenia and as an adjunctive treatment for patients with major depressive disorder (MDD). Brexpiprazole was also approved in 2017 by Health Canada and by the EMA in 2018 in Europe for the treatment of schizophrenia. In addition, brexpiprazole has been approved in several other countries across the world. Brexpiprazole is distributed and marketed under the brand name Rexulti®. In Europe, brexpiprazole is distributed and marketed under the brand name Rxulti®.

Brexpiprazole was discovered by Otsuka and is being co-developed by Otsuka and Lundbeck. The efficacy of brexpiprazole may be mediated through a combination of partial agonist activity at serotonin 5-HT<sub>1A</sub> and dopamine D<sub>2</sub> receptors, and antagonist activity at serotonin 5-HT<sub>2A</sub> receptors. Brexpiprazole exhibits high affinity (sub-nanomolar) for these receptors as well as for noradrenaline alpha1B/2C receptors.

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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 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 17.2 billion in 2017 (EUR 2.3 billion; USD 2.6 billion).

For additional information, we encourage you to visit our corporate site [www.lundbeck.com](http://www.lundbeck.com) and connect with us on Twitter at @Lundbeck.

## About Otsuka Pharmaceutical Co., Ltd.

Otsuka Pharmaceutical is a global healthcare company with the corporate philosophy: "Otsuka-people creating new products for better health worldwide." Otsuka researches, develops, manufactures and markets innovative products, with a focus on pharmaceutical products for the treatment of diseases and nutraceutical products for the maintenance of everyday health.

In pharmaceuticals, Otsuka is a leader in the challenging area of mental health and also has research programs on several under-addressed diseases including tuberculosis, a significant global public health issue. These commitments illustrate how Otsuka is a "big venture" company at heart, applying a youthful spirit of creativity in everything it does.

Otsuka Pharmaceutical is a subsidiary of Otsuka Holdings Co., Ltd. headquartered in Tokyo, Japan. The Otsuka group of companies employed 46,000 people worldwide and had consolidated sales of approximately USD 11,1 billion (€ 9.8 billion) in 2017.

All Otsuka stories start by taking the road less travelled. Learn more about Otsuka Pharmaceutical Company on its global website at <https://www.otsuka.co.jp/en>.



### 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.

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<sup>1</sup> Yehuda R et al. Post-traumatic stress disorder. Nat Rev Dis Primers. 2015;1:15057