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Press release

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Idalopirdine granted Fast Track Designation by U.S. Food and Drug Administration (FDA)

Designation provides the opportunity for more frequent interactions with FDA during clinical development and potential eligibility for priority review

H. Lundbeck A/S (Lundbeck) and Otsuka Pharmaceutical Development & Commercialization, Inc. today announced that the U.S. Food and Drug Administration (FDA) has granted Fast Track Designation to the investigational agent idalopirdine for the treatment of mild to moderate Alzheimer's disease.

Idalopirdine is a selective 5HT6 receptor antagonist with a different hypothesized mechanism of action than currently available Alzheimer's medications. Notably, a focus on the 5-HT6 receptor is a different approach from the amyloid and tau hypotheses that have underpinned much of the drug research to date on Alzheimer's disease.

"We are pleased about the opportunity for priority review for idalopirdine and potentially provide a new option for patients in the battle against Alzheimer's disease, for which there still are substantial unmet needs," said Anders Gersel Pedersen, Executive Vice President and Head of R&D at Lundbeck. "Lundbeck and Otsuka are committed to developing an innovative portfolio of drugs to tackle symptoms of Alzheimer's disease and the FDA Fast Track designation may secure a smoother and faster regulatory process to help us meet that goal."

Four clinical phase III studiesⁱ are underway investigating idalopirdine as an adjunctive symptomatic therapy for patients with mild to moderate Alzheimer's disease. Clinical phase III development was initiated in October 2013 and the program is expected to enroll approximately 2,500 patients worldwide.

Lundbeck and Otsuka will support a symposium titled "Emerging Trends in Alzheimer's Disease, the Rationale for Combination Treatments" and present three posters on idalopirdine at the Alzheimer's Association International Conference (AAIC) that will take place from July 24 to 28 in Toronto, Canada.

About Fast Track Designation

FDA's Fast Track Designation is designed to facilitate the development and expedite the review of drugs intended to treat serious conditions and with the potential to address an unmet medical need.

Companies that receive Fast Track Designation are provided the opportunity for more frequent interactions with FDA during clinical development and are potentially eligible for accelerated approval and/or priority review, if relevant criteria are met.

Additionally, companies that receive Fast Track designation are allowed to submit completed sections of their New Drug Application (NDA) for the drug on a rolling basis, resulting in the potential for an expedited FDA review process.

About idalopirdine

Idalopirdine is a selective 5-HT₆ receptor antagonist. The 5-HT₆ receptor is expressed in brain regions involved in cognition, such as the cortex and the hippocampus, and modulates activity of multiple neurotransmitter systemsⁱⁱ.

Through 5-HT₆ receptors expressed on glutamatergic neurons and GABAergic interneurons, idalopirdine is believed to modulate the balance between excitation (glutamate) and inhibition (GABA) in the brainⁱⁱⁱ. When administered together with donepezil, idalopirdine potentiates the effects of the AChEI on ACh levels and on neuronal activity in the cortex and hippocampus^{iv v}.

Positive results of a 24-week clinical phase II trial with idalopirdine as adjunctive therapy in moderate Alzheimer's disease have been presented^{vi} and to confirm the phase II findings, a large idalopirdine phase III program as adjunct to acetylcholinesterase inhibitors in mild-moderate AD patients is ongoing¹.

About Alzheimer's disease

Alzheimer's disease is a progressive brain disorder in which the brain gradually degenerates. It most frequently occurs in people above 65 years of age. People with Alzheimer's disease develop distressing changes in memory, thought, function and behavior, which worsen over time. These changes increasingly impact the person's daily life and reduce their independence until ultimately these patients are entirely dependent on others^{vii}.

Alzheimer's disease also has an enormous impact on the patient's caregiver. Most caregivers are close relatives who provide care at home — a demanding and exhausting role that represents a significant emotional and physical burden.

Worldwide, 47.5 million people have dementia. Every year, there are 7.7 million new cases. The total number of people with dementia is projected to 75.6 million in 2030 and almost triple by 2050 to 135.5 million^{viii}. Alzheimer's disease is the most common cause of dementia, accounting for 60 to 80% of these patients.^{vii}

Dementia has significant social and economic implications in terms of direct medical costs, direct social costs and the costs of informal care. In 2010, the total global societal costs of dementia were estimated to be US\$ 604 billion. This corresponds to 1.0% of the worldwide gross domestic product (GDP) or 0.6% if only direct costs are considered. The total cost as a proportion of GDP varied from 0.24% in low-income countries to 1.24% in high-income countries^{viii}.

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About Lundbeck

H. Lundbeck A/S (LUN.CO, LUN DC, HLUY) 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 depression, schizophrenia, Parkinson's disease and Alzheimer's disease.

An estimated 700 million people worldwide are living with psychiatric and neurological disorders 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 psychiatric and neurological disorders – we call this Progress in Mind.

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

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 research centres in China and Denmark and production facilities in China, Denmark, France and Italy. Lundbeck generated revenue of DKK 14.6 billion in 2015 (EUR 2 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 Otsuka Pharmaceutical Development & Commercialization, Inc.

Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC), based in Princeton, New Jersey, and Rockville, Maryland, discovers and develops new compounds that address urgent, unanswered medical needs and advance human health. With a strong focus on neuroscience, oncology, and cardio-renal treatments, OPDC is dedicated to improving the

health and quality of human life. For more information, visit www.otsuka-us.com and connect with us on Twitter at @OtsukaUS.

OPDC is a subsidiary of Otsuka America, Inc. (OAI), a holding company established in the U.S. in 1989. OAI is wholly owned by Otsuka Pharmaceutical Co., Ltd. The Otsuka Group employs approximately 47,000 people globally and its products are available in more than 80 countries worldwide. Otsuka welcomes you to visit its global website at <http://www.otsuka.co.jp/en/index.php>.

ⁱ Clinicaltrials.gov. STARSHINE (NCT01955161), STARBEAM (NCT02006641), STARBRIGHT (NCT02006654), STAR Extension (NCT02079246)

ⁱⁱ Yun H. and Rhim H. The Serotonin-6 Receptor as a Novel Therapeutic Target. *Experimental Neurobiology* 2011; 20(4): 159-168

ⁱⁱⁱ Helboe L, Egebjerg J, De Jong IE (2015) Distribution of serotonin receptor 5-HT6 mRNA in rat neuronal subpopulations: A double in situ hybridization study. *Neuroscience* 310, 442-454.

^{iv} Foraster MA et al. (2016) The 5-HT6 receptor antagonist idalopirdine potentiates the effects of donepezil on gamma oscillations in the frontal cortex of anesthetized and awake rats without affecting sleep-wake architecture. Submitted to *J. Neuropharmacology*.

^v Herrik KF et al. (2016) The 5-HT6 receptor antagonist idalopirdine potentiates the effects of acetylcholinesterase inhibition on neuronal network oscillations and extracellular acetylcholine levels in the rat dorsal hippocampus. *Neuropharmacology* 107, 351-363.

^{vi} Wilkinson D, Windfeld K, Colding-Jørgensen E. Safety and efficacy of idalopirdine, a 5-HT6 receptor antagonist, in patients with moderate Alzheimer's disease (LADDER): a randomised, double-blind, placebo-controlled phase 2 trial. *Lancet Neurol* 2014; 13: 1092-99.

^{vii} Alzheimer's Association Report, 2016 Alzheimer's disease facts and figures, *Alzheimer's & Dementia* 12 (2016) 459-509.

^{viii} WHO: <http://www.who.int/mediacentre/factsheets/fs362/en/>