Phase II clinical data show statistically significant improvement for Lu AE58054 as add-on to donepezil, versus donepezil alone, on cognitive symptoms of Alzheimer’s disease

Lundbeck and Otsuka present data at Alzheimer’s Association International Conference 2013

- Lu AE58054 is a selective 5-HT6 receptor antagonist under investigation for the treatment of Alzheimer’s disease
- Lundbeck and Otsuka will initiate a phase III clinical program in about 3,000 patients during the second half of 2013
- The two companies’ focus on the 5-HT6 receptor is a different approach from the amyloid and tau hypotheses that have underpinned much of the research to date on Alzheimer’s disease
- 36 million people worldwide are estimated to have dementia, with the number expected to almost double every 20 years


The phase II clinical study demonstrated that treatment with Lu AE58054 as add-on to donepezil for six months improved cognitive performance in patients with moderate Alzheimer’s disease.

“I am very pleased with the data achieved in this project. Lu AE58054 potentially represents a new approach to Alzheimer’s disease and a continuation of Lundbeck’s commitment to addressing this complicated disease”, says Executive Vice President Anders Gersel Pedersen, Head of Research & Development at Lundbeck. “It is my hope that the clinical phase III program will confirm results seen from this phase II trial, and demonstrate a positive outcome on this devastating disease”.

William H. Carson, M.D., President and Chief Executive Officer, Otsuka Pharmaceutical Development and Commercialization, Inc., notes that “Our investigation of the 5-HT6 receptor and its role in memory processes and in Alzheimer’s disease is encouraging. We are eager to continue phase III trials with Lundbeck”.

About the study
This phase II clinical study exploring the efficacy and safety of Lu AE58054 as add-on to donepezil was a multi-center, randomized, double-blind, parallel-group, placebo-controlled trial for a period of 24 weeks. The study was conducted in 278 patients with moderate Alzheimer’s disease in Europe, Canada and Australia.

Lu AE58054 plus donepezil demonstrated significant improvements in cognitive function in Alzheimer’s disease compared to placebo plus donepezil:
A Clinical Phase II Study of Lu AE58054 Added to Stable Donepezil Treatment in Patients with Moderate Alzheimer’s Disease (AAIC 2013 oral presentation):

- Addition of Lu AE58054 (90 mg/day) to stable donepezil treatment resulted in improved cognitive performance as measured by the primary endpoint ADAS-Cog at Week 24 (p=0.004). The mean difference in ADAS-Cog at Week 24 was -2.16 (95% confidence interval of -3.62 to -0.69). The effect was apparent after 12 weeks.
- Secondary efficacy assessments including ADCS-CGIC and ADCS-ADL showed a trend in favor of Lu AE58054 treatment at Week 24 compared with patients who only received donepezil, but the differences were not statistically different. The study was not designed to show statistically significant differences for these secondary endpoints.
- Treatment with Lu AE58054 was generally well tolerated. Liver enzyme (ALT, AST, GGT) elevations were observed in some patients. Changes in transaminases were asymptomatic and returned towards baseline values in patients who either continued treatment or withdrew from the study.

Following the AAIC, an abstract of the 16 July presentation will be published in Alzheimer's and Dementia: The Journal of the Alzheimer's Association.

In the second half of 2013, the phase III clinical program is expected to commence. The program is currently planned to enroll approximately 3,000 patients with Alzheimer’s disease. Several doses of Lu AE58054 will be used in combination with donepezil in order to explore in mild-to-moderate dementia of the Alzheimer’s type as adjunctive therapy to acetylcholinesterase inhibitors (AChEIs). The program will enroll patients globally and is expected to last up to three years.

About Lu AE58054
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 systems. Lu AE58054 is a selective 5-HT6-receptor antagonist. In pre-clinical models, Lu AE58054 was shown to improve cognition and enhance the effects of the acetylcholinesterase inhibitor donepezil on hippocampal function. A number of early trials have demonstrated that a 5-HT6-receptor antagonist could offer potential benefits in the treatment of disorders such as Alzheimer's disease and in November 2009 Lundbeck initiated the above described 24 week clinical phase II trial with Lu AE58054 as adjunctive therapy in Alzheimer’s disease.

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.

Alzheimer's disease is associated with brain shrinkage and disruptions in the activity of neurotransmitters. As the brain degenerates, characteristic waste accumulates in the brain, known as 'plaques' and 'tangles'.
The largest development efforts to date on investigational drugs for Alzheimer’s have focused on reducing amyloid plaque formation or excessive phosphorylation of tau proteins.iii The blocking of 5HT6 receptors represents an alternative, potentially promising approach.viii

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.x

Worldwide, it is estimated that about 36 million people have dementia. With the shift towards an increasingly elderly population, it is predicted that the number of people affected by dementia will almost double every 20 years, and by the year 2050, 115 million people will have the condition.iv,v Alzheimer’s disease is the most common cause of dementia, accounting for 50 to 80% of these patients.xi

The worldwide costs of dementia (USD 604 billion in 2010) amount to more than 1% of gross domestic product (GDP).v

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About Otsuka Pharmaceutical Co., Ltd.
Otsuka Pharmaceutical Co., Ltd. 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 and original 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 leading firm in the challenging area of mental health and for several decades has been active in research on tuberculosis, a significant global public health issue. These commitments illustrate more powerfully than words how Otsuka is a “big venture” company at heart, applying a youthful spirit of creativity in everything it does.

Otsuka is a wholly owned subsidiary of Otsuka Holdings Co., Ltd., the holding company for the Otsuka Group. The chairman Akihiko Otsuka is the third generation of Otsuka family members to lead the business, whose origins date from 1921. The Otsuka Group has business operations in 25 countries and regions around the world, with consolidated sales of approximately USD 13 billion (approximately EUR 10 billion) for fiscal year 2012 (4/1/2012-3/31/2013.) Otsuka welcomes you to visit its global website at https://www.otsuka.co.jp/en /
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 “HLUYY”. For additional information, we encourage you to visit our corporate site www.lundbeck.com.

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References:


vii. ALT=alanine aminotransferase; AST=aspartate aminotransferase


