H. Lundbeck A/S

Ottiliavej 9
DK-2500 Valby, Denmark

Tlf +45 36 30 13 11
Fax +45 36 43 82 62

E-mail information@lundbeck.com
www.lundbeck.com

Press release

For non-US media

Valby, 23 June 2015

Young adult patients* with schizophrenia show improved functioning and health-related quality of life with Abilify Maintena® (aripiprazole once-monthly) compared with paliperidone palmitate

- **A newly released pre-specified subgroup analysis from the QUALIFY** study shows that younger adult patients* improve significantly on aripiprazole once-monthly compared with paliperidone palmitate as measured by the Heinrichs-Carpenter Quality of Life Scale (QLS).[1]**
- **The positive effect of aripiprazole once-monthly is seen consistently in this subgroup of younger patients* across a range of effectiveness measures, suggesting that aripiprazole once-monthly treatment at a younger age may confer better treatment outcomes than paliperidone palmitate in patients with schizophrenia.[1]**
- **Results from this pre-defined subgroup analysis, and on additional secondary and other endpoints of the study were presented for the first time at the American Society of Clinical Psychopharmacology (ASCP), 2015 Annual Meeting in Miami, United States (22–25 June).[1]**

Otsuka Pharmaceutical Europe Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) announced today that a newly released subgroup analysis of data from the QUALIFY study showed significantly greater and clinically meaningful improvements in functioning and health-related quality of life (HRQoL) with aripiprazole once-monthly compared with paliperidone palmitate in patients aged 18-35 years living with schizophrenia[1].

A difference in improvement in QLS total scores between aripiprazole once-monthly and paliperidone palmitate of 10.7 points was observed in patients aged 18-35 years (p=0.037).[1] Changes of more than five points in the QLS total scores are considered clinically meaningful, i.e. physicians should be able to notice these changes in their patients in clinical practice.[2,3] Superiority of aripiprazole once-monthly compared with paliperidone palmitate in the study's primary endpoint was also observed in the total QUALIFY study population (difference in change of 4.7 points, p=0.036).[4] The positive effect of aripiprazole once-monthly compared with paliperidone palmitate in the subgroup of patients aged 18-35 years was consistently seen across a range of effectiveness measures (QLS, IAQ, CGI-S). This suggests that treatment with aripiprazole once-monthly may confer better treatment outcomes than with paliperidone palmitate in this patient subgroup.[1]

"*These latest findings from the QUALIFY study are particularly encouraging for young adults with schizophrenia who are in the formative years of their lives, a time during which many complete school, establish a career, build personal relationships, and start a family*,"[1,4] said investigator Steven G. Potkin, of the Department of Psychiatry and Human Behaviour, University of California. "*The study findings indicate that treatment with aripiprazole once-monthly in adult patients aged 35 years and younger may be particularly beneficial in improving these patients' abilities to do better in social, home, and work or education-related environments.*"[1]

The subgroup analysis also showed that younger adult patients* had a significantly greater reduction in disease severity with aripiprazole once-monthly compared with paliperidone palmitate as assessed by the Clinical Global Impression-Severity scale (CGI-S) (mean difference -0.44, p=0.026), and showed significantly greater relative effectiveness as assessed by the Investigator's Assessment Questionnaire (IAQ) (mean difference -2.65, p=0.048).[1]

Among patients over the age of 35 years, improvements in the QLS, CGI-S and IAQ were also observed, with total score improvement numerically greater with aripiprazole once-monthly than with paliperidone palmitate, though the differences were not statistically significant at week 28.[1]

Notes to Editors:

About the QUALIFY Study

QUALIFY is a 28-week, randomized, open-label, rater-blinded, head-to-head comparison of aripiprazole once-monthly (400 or 300 mg/month)) and intramuscular paliperidone palmitate (50 to 150 mg/month in the EU and Canada or equivalent 78 to 234 mg/month in the US).[4,5] After a three-week oral conversion period when patients received either oral aripiprazole or oral paliperidone, the intramuscular formulations were administered according to approved local instructions (EU Summary of Product Characteristics or US Package Insert)[6,7] for five weeks and continued for 20 weeks.[4,5] The study included 295 patients (78 patients were aged 18-35 years) in Europe and North America who needed a change from their current oral antipsychotic treatment.[5]

The primary endpoint assessed non-inferiority and subsequently superiority on change from baseline to week 28 in Heinrich-Carpenter Quality of Life Scale (QLS) total score.[8,†] The QLS is a health-related quality of life scale focused on intrapsychic, social, and negative symptoms, and their consequences on quality of life in schizophrenia. The purpose of the scale is to examine a patient's social experience, work functioning, sense of purpose, motivation, and level of participation in the community.[8,9] The primary endpoint results showed a statistically significant difference in improvement from baseline to week 28 on QLS total score[4] (mean difference of 4.7, p=0.036), demonstrating non-inferiority to paliperidone palmitate and establishing superiority of aripiprazole once-monthly to paliperidone palmitate by pre-specified criteria.[4]

On the secondary endpoints in the total population, from baseline to week 28, aripiprazole once-monthly gave greater reduction than paliperidone palmitate in disease severity (CGI-S) as rated by the clinician (mean treatment difference: -0.28, p=0.004) and greater improvements in relative effectiveness (IAQ) (mean difference -1.49, p=0.043) in the total study population; improvements were also seen in patients' readiness to work as assessed by the WoRQ scale (odds ratio: 2.67, 95%CI:[1.39;5.14], p=0.003), in a post-hoc analysis of this scale, 26% of patients on aripiprazole once-monthly changed from 'no' to 'yes' on readiness to work compared with 12% of patients on paliperidone palmitate (p=0.003).[1] The WoRQ scale measures the capacity of patients with schizophrenia to engage in compensated work.[10.] The CGI-S provides global measures of the severity of a patient's clinical condition.[11] The IAQ assesses the relative effectiveness (efficacy, safety, and tolerability) of antipsychotic medications in patients with schizophrenia or schizoaffective disorder.[12]

In the QUALIFY study, both treatments were generally well-tolerated; discontinuation rates due to adverse events were 11.1% with aripiprazole once-monthly [n=16/144] and 19.7% with paliperidone

palmitate [n=27/137]. The most common treatment-emergent adverse events with greater than five percent incidence in either group during the maintenance treatment continuation phase were respectively for aripiprazole once-monthly vs paliperidone palmitate: weight increase (10.1% vs 15.6%, psychotic disorder (2.5% vs 5.5%) and insomnia (2.5% vs 5.5%).[4]

* Aged 18-35 years
** Quality of Life with Abilify Maintena Study
† The Quality of Life Scale (QLS) was designed to assess deficit symptoms of schizophrenia, and functioning during the preceding four weeks.

About Abilify Maintena® (aripiprazole once-monthly)
Aripiprazole once-monthly is the only long-acting injectable (LAI) antipsychotic that exerts partial agonist activity at the D2 dopamine receptor. In European Union aripiprazole once-monthly is indicated for maintenance treatment of schizophrenia in adult patients stabilized with oral aripiprazole (indication might differ and must be checked for other countries). Aripiprazole once-monthly is a once-monthly formulation of aripiprazole in a sterile lyophilized powder that is reconstituted with sterile water and the recommended starting and maintenance dose is 400mg. After the first injection, treatment with 10 mg to 20 mg oral aripiprazole should be continued for 14 consecutive days to maintain therapeutic aripiprazole concentrations during initiation of therapy.[6,7]

Following the initial approval in 2013, aripiprazole once-monthly is now available in 26 countries including the US, UK, Germany, Spain, Italy, France, Canada and Australia.

Lundbeck contact for media:
Mads Kronborg, Director, Media Relations
Telephone (direct): +45 36 43 28 51

Otsuka contact for media:
Alison Ross, Head of communication
aross@otsuka-europe.com
Telephone: +44 7768 337128

About the Otsuka and Lundbeck Global Alliance
Otsuka and Lundbeck established a global alliance in November 2011 to bring to bear their considerable experience and resources in the CNS area to introduce next-generation treatments for conditions such as schizophrenia, depression, Alzheimer's disease and alcohol dependency.

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 research within neuroscience.
Our key areas of focus are alcoholic dependence, Alzheimer's disease, bipolar disorder, depression/anxiety, epilepsy, Huntington's disease, Parkinson's disease, schizophrenia and symptomatic neurogenic orthostatic hypotension (NOH).
An estimated 700 million people worldwide are living with brain disease 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 disease – we call this Progress in Mind.

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

About Otsuka

Otsuka Pharmaceutical Co., Ltd. is a global healthcare company with the corporate philosophy: 'Otsuka-people creating new products for better health worldwide.'

At Otsuka the emphasis is on 'super people' who have a flair for the unconventional not 'super computers'. This has led us to become a leading firm in the challenging area of mental health. Beyond mental health, this thinking has resulted in the development of first-in-class products to treat kidney, cardiovascular and gastrointestinal disorders and blood-related cancers. Otsuka also has research programmes for several under-addressed diseases including tuberculosis, a significant global public health issue. The Otsuka Group employs approximately 43,000 people globally.

Otsuka Pharmaceutical Europe Ltd. was established in 1979. Our 600 European employees focus their passion and energy into ensuring that patients have access to Otsuka's new products, including in 2015 the first-ever drug treatment in Europe for polycystic kidney disease. Otsuka also received approval in 2014 for the first new anti-tuberculosis drug in Europe in over 40 years.

Our stories all start by taking the road less travelled. Learn more here: www.otsuka.co.jp/en/ (Global) and www.otsuka-europe.com (European).

REFERENCES:

1. Naber, D., et al. *Secondary effectiveness outcomes in QUALIFY, a head-to-head clinical study of aripiprazole once monthly and paliperidone palmitate in schizophrenia*. Poster 87. Presented at American Society of Clinical Psychopharmacology (ASCP), 2015 Annual Meeting; 22–25 June 2015. Miami, Florida, USA.
2. Jones, P.B., et al. Randomized controlled trial of the effect of quality of life of second- vs first-generation antipsychotic drugs in schizophrenia. *Arch Gen Psychiatry*. 2006.63:1079-87.
3. Falissard B, et al. Defining the minimal clinically important difference of the Heinrichs-Carpenter Quality of Life Scale (QLS). *Int J Methods Psychiatr Res.* 2015 (in press)
4. Naber, D., et al. *Ariprazole once-monthly is superior to paliperidone palmitate in a randomized, head-to-head clinical study*. Presented at the 23rd European Congress of Psychiatry (EPA); 28–31 March 2015. Vienna, Austria.
5. QUALIFY study (NCT01795547) Aripiprazole Once-monthly Versus Paliperidone Palmitate in Adult Patients With Schizophrenia 2013. [Accessed at: June 2015; Available from: clinicaltrials.gov. https://clinicaltrials.gov/ct2/show/NCT01795547.]
6. European Medicines Agency (EMA). Abilify Maintena® Summary of Product Characteristics. 2015. [Accessed at: May 2015; Available from: http://www.ema.europa.eu/ema/.]
7. US Food and Drug Administration (FDA). Abilify Maintena® Prescribing Information. 2014. [Accessed at: June 2015; Available from: http://www.accessdata.fda.gov/.]
8. Heinrichs, D.W., et al. The Quality of Life scale: An instrument for rating the schizophrenic deficit syndrome. *Schizophr Bull*. 1984.10:388–98.
9. Fervaha, G. et al. Validation of an abbreviated quality of life scale for schizophrenia. *Eur Neuropsychopharmacol*. 2013.9:1072-77.
10. Potkin SG., et al. Psychometric evaluation of the Work Readiness Questionnaire in schizophrenia. *CNS Spectr*. 2014. 1–8: [Epub ahead of print].
11. Guy, W. ECDEU assessment manual for psychopharmacology. Rockville, MD: National Institute of Mental Health (US), 1976.

12. Tandon R., et al. IAQ Validation Study Group. Validation of the Investigator's Assessment Questionnaire, a new clinical tool for relative assessment of response to antipsychotics in patients with schizophrenia and schizoaffective disorder. *Psychiatry Res*. 2005. 136(2–3): 211–221.