

Press release

Valby, 23 March 2017

Lundbeck and Otsuka's brexpiprazole for adult patients with schizophrenia accepted for review by EMA

The European Medicines Agency (EMA) is expected to complete its review in second quarter of 2018. In both short-term and long-term clinical trials involving more than 3,000 patients, brexpiprazole has shown improvement in symptoms of schizophrenia and was generally well-tolerated in adult patients.

H. Lundbeck A/S (Lundbeck) and Otsuka Pharmaceutical Co., Ltd. (Otsuka) today announce that the European Medicines Agency (EMA) has accepted for review a Marketing Authorisation Application for brexpiprazole to treat schizophrenia in adults.

Brexpiprazole is a once-daily, second-generation (atypical) oral antipsychotic that was discovered by Otsuka and co-developed by Otsuka and Lundbeck. The mechanism of action for brexpiprazole in the treatment of schizophrenia is unknown. However, the efficacy of brexpiprazole may be mediated through a combination of partial agonist activity at serotonin 5-HT_{1A} and dopamine D₂ receptors, and antagonist activity at serotonin 5-HT_{2A} receptors. In addition, brexpiprazole exhibits high affinity (subnanomolar) for these receptors as well as for noradrenaline alpha_{1B/2C} receptorsⁱ.

The application is supported by data from five phase III placebo-controlled clinical trials in adult subjects with schizophrenia including two multinational, six-week, randomized trials and a 52-week randomized maintenance trial^{ii,iii,iv}.

The EMA is anticipated to complete its review in second quarter of 2018.

Schizophrenia is a chronic, severe and disabling brain condition. Typically, symptoms are first seen in adults younger than 30 years of age and include hearing voices, believing other people are reading their minds or controlling their thoughts, and being suspicious or withdrawn. In Europe, it is estimated that there are about 5 million people with schizophrenia, with a prevalence of 0.6-0.8%^v.

Brexpiprazole was approved by the U.S. Food and Drug Administration in July 2015 to treat patients with schizophrenia (as well as an adjunctive treatment of major depressive disorder (MDD)). Brexpiprazole was also approved in February 2017 by Health Canada for the treatment of schizophrenia. In both countries brexpiprazole is distributed and marketed under the brand name REXULTI[®]. If the EMA grants regulatory approval to brexpiprazole, the brand name of the product in the EU would be RXULTI[®].

Contacts

Lundbeck
Mads Kronborg
Senior Director, Corporate Communication
Phone: +45 36 43 40 00
E-mail: mavk@lundbeck.com

Otsuka, Europe
Alison Ross
Otsuka Pharmaceutical Europe Ltd.
aross@Otsuka-Europe.com
+44 7768337128

Otsuka, Japan
Jeffrey Gilbert
Otsuka Pharmaceutical Co, Ltd.
gilbert.jeffrey@otsuka.co.jp
+81 3 6361 7379, +81 80 8728 6039

About Lundbeck

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 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, production, 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 15.6 billion in 2016 (EUR 2.1 billion; USD 2.3 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

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

The Otsuka group of companies employs approximately 45,000 people globally. Otsuka Pharmaceutical Europe's 600 employees channel their passion and energy into ensuring that the latest science is converted into needed therapies for patients with mental health disorders; kidney, cardiovascular, gastrointestinal and infectious diseases; and blood related cancers. Our stories all start by taking the road less travelled. Learn more here:
www.otsuka.co.jp/en/ <<http://www.otsuka.co.jp/en/>> (Global)
www.otsuka-europe.com <<http://www.otsuka-europe.com>> (Europe)

References

-
- ⁱ Maeda K, Sugino H, Akazawa H, et al. Brexpiprazole I: in vitro and in vivo characterization of a novel serotonin-dopamine activity modulator. *J Pharmacol Exp Ther.* 2014b; 350(3):589–604.
- ⁱⁱ Correll, C., Skuban, A, Ouyang, J., et al. Efficacy and safety of Brexpiprazole for the treatment of acute schizophrenia: A 6-week randomized, double-blind, placebo-controlled trial. *Am J Psychiatry* 2015; 172:870–880; doi: 10.1176/appi.ajp.2015.14101275
- ⁱⁱⁱ Kane J. a, Skuban A., Ouyang J. et al. A multicenter, randomized, double-blind, controlled phase 3 trial of fixed-dose brexpiprazole for the treatment of adults with acute schizophrenia. *Schizophrenia Research* 164 (2015) 127–135
- ^{iv} Fleischhacker, W., Hobart, M., Ouyang J., et al. Efficacy and safety of brexpiprazole (OPC-34712) as maintenance treatment in adults with schizophrenia: A randomized, double-blind, placebo-controlled study. *Int. Journal of Neuropsychopharmacology* (2017) 20(1) : 11-21
- ^v C. Altamura, A. Fagiolini, S. Galderisi, P. Rocca, A. Rossi. Schizophrenia today: epidemiology, diagnosis, course and models of care. *Journal of Psychopathology* 2014;20:223-243.