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For Immediate Release

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Otsuka and Lundbeck's Rxulti® (brexpiprazole) receives positive opinion in EU from CHMP for the treatment of schizophrenia in adults

Otsuka Pharmaceutical Co., Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) announce that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion on Rxulti® (brexpiprazole) for the treatment of schizophrenia in adult[*1] on June 1, 2018. A final decision from the European Commission is expected within 67 days.

Brexpiprazole is a once-daily second generation (atypical) oral antipsychotic; it provides a combination of partial agonist activity at serotonin 5-HT_{1A} and dopamine D_2 receptors, and antagonist activity at serotonin 5-HT_{2A} receptors.[*2] Brexpiprazole exhibits high affinity for these receptors as well as for noradrenaline alpha$_{1B/2C}$ receptors.[*2]

The submission to the EMA included efficacy and safety data of brexpiprazole in schizophrenia from six placebo-controlled clinical trials.[*3, *4, *5, *6, *7, *8] The safety data were further included from a large cohort of patients evaluated in four long-term, open-label trials which included patients rolled over from the short-term trials as well as patients with no prior exposure to brexpiprazole.[*9]

The phase 3 efficacy trials comprise three short-term, phase 3, fixed-dose trials;[*3, *4, *5] one phase 3, short-term, flexible-dose trial with quetiapine as active reference;[*6] and one phase 3, long-term maintenance (relapse-prevention) trial.[*7] In the three fixed-dose, short-term trials (trials one, two and three), subjects were randomised to brexpiprazole 0.25 mg once daily, 1 mg once daily, 2 mg once daily, 4mg once daily or placebo.[*3, *4, *5] Trial four assessed the efficacy, safety, and tolerability of brexpiprazole in a flexible dose range of 2 to 4 mg/day and 400 to 800mg quetiapine XR for assay sensitivity.[*6] In the short-term trials, the primary efficacy endpoint was defined as the mean change from baseline to week 6 in Positive and Negative Syndrome Scale (PANSS) total scores.[*3, *4, *5]

In the long-term trial designed to assess the maintenance of effect of brexpiprazole by assessing the delay in time to impending relapse of schizophrenia, brexpiprazole demonstrated a significantly longer time to relapse compared with patients on placebo ($p < 0.0001$).[*7]

Together, the trials demonstrated that brexpiprazole is an effective and well-tolerated treatment for schizophrenia.[*3, *4, *5, *7, *8, *9]

Brexpiprazole was discovered by Otsuka and is being co-developed by Otsuka and Lundbeck. Following the European Commission's final decision, Otsuka and Lundbeck will work with local pricing and reimbursement bodies in countries throughout Europe to help ensure that eligible patients are able to access this medicine.

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*1 European Medicines Agency Committee for Medicinal Products for Human Use (CHMP), June 2018. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Summary_of_opinion_-_Initial_authorisation/human/003841/WC500249801.pdf [Accessed: June 2018].

*2 Maeda K, et al. *J Pharmacol Exp Ther.* 2014b; 350(3): 589–604.

*3 Correll C, et al. *Am J Psychiatry*. 2015; 172(9): 870–880.

*4 Kane J, et al. *Schizophr Res*. 2015; 164: 127–135.
*5 Ishigooka J, et al. *Psychiatry and Clinical Neurosciences*. 2018; Available from: doi/pdf/10.1111/pcn.12682 [Accessed: June 2018].
*6 Marder SR, et al. *Acta Neuropsychiatrica*, 2016; 29(5): 278–290.
*7 Fleischhacker W, et al. *Int J Neurophamacol*. 2017 Jan; 20(1): 11–21. Available from: doi: 10.1093/ijnp/pyw076 [Accessed: June 2018].
*8 Correll C, et al. *Schizophr. Res*. 2016 Jul; 174(1-3): 82–92. doi: 10.1016/j.schres.2016.04.012. Epub 2016 May 4. [Accessed: June 2018].
*9 Kane J, et al. *Schizophr Res*. 2016 Jul; 174(1-3): 93–98. doi: 10.1016/j.schres.2016.04.013. Epub 2016 May 14. [Accessed: June 2018].