June 17, 2014

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Termination of the license agreement for ONO-4641 mutually agreed by Ono and Merck

Ono Pharmaceutical Co., Ltd. (Osaka, Japan, "Ono") announced today it has reached an accord with Merck (Darmstadt, Germany) to terminate the license agreement for ONO-4641, which was executed on October 3, 2011 (the "Agreement").

ONO-4641 is a sphingosine-1-phosphate (S1P) receptor agonist discovered and developed by Ono. Merck obtained an exclusive license for development and commercialization of ONO-4641 in countries around the world except Japan, Korea and Taiwan, and both companies had developed ONO-4641 for multiple sclerosis thereafter. While ONO-4641 met the primary endpoint (the reduction of cumulative number of MRI lesions) in the global Phase II study in relapsing-remitting multiple sclerosis patients, both companies agreed to terminate the Agreement comprehensively considering the significant change in market circumstances of multiple sclerosis treatment, large and extensive Phase III studies required and, as a result, NDA filing of ONO-4641 delayed. Merck will return the license for ONO-4641, and Ono will explore any further development of ONO-4641.
By this termination of the Agreement, there is no change on the Ono's financial forecast of this fiscal year (ending March 2015).

(Reference)

Released on April 17, 2012

ONO-4641 Met Primary Endpoint of Phase II Study in Multiple Sclerosis Patients

The study was a double-blind placebo-controlled study conducted in 11 countries including North America, Europe and Japan in patients with relapsing-remitting multiple sclerosis. A total of 407 patients between the ages of 18 and 55 with relapsing-remitting MS were randomized to receive placebo or one of 3 active doses of ONO-4641 once daily for 26 weeks.
Patients were included in the study if they had two or more relapses in the two years prior to the study, one or more relapses within the year prior to the study or one or more new MS-related

brain lesions, also known as Gd-enhancing lesions, detected on MRI within three months prior to the study. For the primary endpoint of the study, MRIs were performed every four weeks from 10 to 26 weeks, 5 times.

At the end of the study, patients taking 0.05, 0.10, or 0.15 mg of ONO-4641 had 82 percent, 92 percent and 77 percent fewer Gd-enhancing brain lesions (all $p<0.0001$), respectively, compared to placebo.

Adverse events appeared to be generally dose related. Of note was a slower heartbeat and atrioventricular blocks associated with the initiation of treatment, which were asymptomatic, transient and did not require ONO-4641 discontinuation. Other notable adverse events included liver enzyme elevations. In addition, Grade 4 lymphopenia, which is an abnormally low level of lymphocytes in the blood, occurred in 4 percent of patients receiving the 0.15 mg dose of ONO-4641 and in 1 percent of those receiving the 0.10 mg dose.