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*Eisai is a Human Health Care Corporation striving for innovative solutions in prevention, cure and care for the health and well-being of people worldwide. We combine our talents to understand and meet the needs of patients and their families to enhance the quality of life.*

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Eisai Co., Ltd.

# Status of the E2007 (perampanel) Development Program - Termination of Parkinson's Disease Clinical Development and Focus on Neuropathic Pain and Epilepsy Indications -

E2007 (perampanel) is a first-in-class, orally administered, highly selective non-competitive AMPA-type glutamate receptor antagonist, in development by Eisai for several indications, including Parkinson's disease, neuropathic pain, epilepsy, multiple sclerosis and migraine prophylaxis.

The AMPA receptor is widely present in almost all excitatory neuronal synapses. It is believed to play a role in a large number of central nervous system (CNS) diseases with different underlying pathophysiology, including neurodegenerative disorders, movement disorders, pain and psychiatric disorders. Eisai has been pursuing development of perampanel for several CNS indications, some of which are currently in Phase II and Phase III. The most advanced indication is Parkinson's disease for which Eisai has been conducting three global Phase III studies (Studies 301, 302 and 309) with perampanel as add-on therapy to levodopa in patients with late-stage disease. Additionally, Eisai is preparing for global Phase III studies for epilepsy and conducting two Phase II studies for neuropathic pain.

Following the completion of the first Phase III Study 301, we recently completed the second Phase III Study 302, which was primarily conducted in North America. Study 302 is a 20-week, double-blind, placebo-controlled study comparing two doses of 2mg and 4mg of perampanel to placebo. The results, compared with placebo, did not show a significant difference in the primary endpoint of reduction of "off" time (time when signs and symptoms of Parkinson's disease return as the effect of levodopa wears off). Perampanel was generally well tolerated. After analyzing the data, Eisai has decided to discontinue the Parkinson's disease program and not pursue regulatory submissions for this indication. Eisai will focus resources on two other ongoing indications, epilepsy and neuropathic pain, both of which have different pathophysiology from that of Parkinson's disease and robust scientific rationale.

Following the decision to terminate the Parkinson's disease indication, Eisai has also decided to terminate the third Parkinson's disease Phase III study (Study 309) and open label treatment extension studies. Perampanel was generally well tolerated throughout the program in this mostly elderly population. The decision to terminate the Parkinson's disease program is due to lack of efficacy over placebo seen in the recently completed two Phase III studies only, and is not predictive of activity in the other indications including epilepsy and neuropathic pain.

In preclinical models in Parkinson's disease, perampanel improved the effect of levodopa, and a Phase II study suggested that perampanel improved benefits with increasing doses. Responding to unmet medical need, Eisai pursued development of perampanel in Parkinson's disease as a first-in-class oral AMPA antagonist with a non-dopaminergic mechanism, which is different from that of existing drugs. The reason for the lack of statistical significance in effectiveness observed in the two completed Phase III studies for Parkinson's disease is being investigated carefully, but because the mechanism of perampanel is different from that of dopaminergic drugs such as levodopa and dopamine agonists, in-depth review will be necessary.

The pharmacological rationale for perampanel in Parkinson's disease is the therapeutic augmentation of levodopa. However in neuropathic pain and epilepsy, the rationale is to direct parampanel's demonstrated activity as an AMPA receptor antagonist toward inhibition of the neuronal excitability and sensitization caused by glutamate.

Testing in various established animal models has suggested that perampanel has a potential antiepileptic effect. The five animal seizure models tested (maximal electroshock, 6Hz psychomotor, pentylenetetrazole, audiogenic and kindling seizure models) suggested that perampanel may be effective in treating epilepsy. Three Phase II studies (Study 203, 206 and 208), which include doses to be used in Phase III, suggest that perampanel is generally well tolerated with a dose-dependent efficacy in patients with refractory partial seizures.

The most recently completed Phase II Study 208 evaluated maximum tolerated dose (MTD) and safety of perampanel as adjunctive therapy in subjects with refractory partial seizures. This was a 16-week, placebo-controlled, dose-escalation (to a maximum of 12 mg/day), parallel-group study conducted in Europe. Perampanel showed an increasing trend in activity up to 12 mg/day in epilepsy patients with refractory partial seizures. There was a 40% median seizure reduction in the perampanel arm and a 2% median seizure increase in the placebo arm. The responder rate, defined as a proportion of patients with more than 50% seizure reduction, was 40% in the perampanel arm and 22% in the placebo arm.

Eisai is preparing to initiate global Phase III studies with perampanel as add-on therapy in patients with refractory partial seizures in the first quarter of fiscal year 2008. The regulatory submission is planned for fiscal year 2012.

Several pre-clinical models have also suggested that perampanel may be effective in treating neuropathic pain. The Phase II POC Study 227 in painful diabetic neuropathy (PDN) completed enrollment in March and is expected to provide top-line results in September 2008. A Phase III program will start soon afterwards, with regulatory submission for an indication in PDN planned in fiscal year 2010. A Phase II study in a second neuropathic pain indication, post-herpetic neuralgia (PHN), was initiated in January 2008.

Both the Phase III programs in neuropathic pain and in epilepsy plan to investigate a wider range of doses up to 12mg.

Perampanel has been generally well tolerated, as confirmed in the clinical dataset of over 2,300 patients.

Eisai remains strongly committed to the further development of perampanel, as it has the potential to be a well tolerated first-in-class drug for neuropathic pain, epilepsy, and possibly other CNS diseases, with a well differentiated profile of value, for the benefit of many patients and their families.

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**[Please see the attached for the information about the terminology]**

Terminology

(1) Dopaminergic Drug
Dopaminergic drugs such as levodopa and dopamine agonists act directly at dopaminergic receptors, or improve the efficacy of dopamine by regulating its mechanism.

(2) Non-dopaminergic Drug
Drugs that show efficacy by a mechanism other than direct effects on the dopamine receptor or dopamine metabolism. They include the current Parkinson's disease treatments such as anti-cholinergic agents, NMDA inhibitors, etc.