

## **EISAI TO INITIATE TWO PHASE III CLINICAL STUDIES FOR ANTIEPILEPTIC DRUG PERAMPANEL (FYCOMPA®) IN PEDIATRIC PATIENTS WITH PARTIAL-ONSET OR PRIMARY GENERALIZED TONIC-CLONIC SEIZURES AND IN PATIENTS WITH SEIZURES ASSOCIATED WITH LENNOX-GASTAUT SYNDROME**

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today the initiation of respective Phase III clinical studies for its in-house-discovered antiepileptic drug (AED) perampanel (generic name: perampanel hydrate, product name: Fycompa®) as adjunctive therapy in pediatric patients with partial-onset seizures or primary generalized tonic-clonic seizures (Study 311) and in patients with seizures associated with Lennox-Gastaut syndrome (LGS, Study 338).

Study 311 is a global multicenter, single-arm Phase III clinical study of perampanel in approximately 160 patients (ages 4 to less than 12 years) with inadequately controlled partial-onset seizures or primary generalized tonic-clonic seizures. However, in Japan, only patients with partial-onset seizures will be included. The study will evaluate the safety, tolerability, and exposure-efficacy relationship of perampanel when administered as an adjunctive therapy.

Study 338 is a global multicenter, randomized, placebo-controlled, double-blind Phase III clinical study of perampanel in approximately 140 patients at least 2 years of age with inadequately controlled seizures associated with LGS. The study will evaluate whether perampanel, when given as adjunctive therapy, is superior to placebo.

Epilepsy affects approximately 1 million people in Japan, 2.9 million people in the United States, 6 million people in Europe, and approximately 60 million people worldwide. While epilepsy affects people of all ages, incidence is particularly high among children and the elderly. As approximately 30% of patients with epilepsy are unable to control their seizures with currently available AEDs,<sup>1</sup> this is a disease with significant unmet medical need.

LGS is one of the most severe and intractable forms of childhood-onset epilepsy. Characterized by multiple seizure types, the disorder is extremely difficult to control, with patients normally having to take several different AEDs. Seizures associated with LGS lead to falls due to sudden loss of consciousness. LGS often causes delayed intellectual development and behavioral disturbances, and therefore has a significant impact on the quality of life of both patients and their families.

Perampanel is a first-in-class AED discovered at Eisai's Tsukuba Research Laboratories. It is a highly selective, noncompetitive AMPA receptor antagonist that reduces neuronal hyperexcitation associated with seizures by targeting glutamate activity at postsynaptic AMPA receptors. Perampanel is available in tablet form to be taken once daily, and an oral suspension formulation has been approved in the United States and Europe. It is approved in countries around the world as an adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures, and primary generalized tonic-clonic seizures in patients with epilepsy 12 years of age and older.

In addition, Eisai has submitted a supplemental application for a partial label change for perampanel as monotherapy for treatment of partial-onset seizures in patients with epilepsy 12 years of age and older based on new U.S. Food and Drug Administration policy.

Together with the worldwide provision of Fycompa, Eisai is striving to continuously create new medicines for the field of epilepsy. In addition, Eisai is promoting initiatives such as provision of the EMILY epilepsy support app with SOS and communication functionality in Japan to address the diverse needs of patients with epilepsy and their families around the world.

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**[Notes to editors]**

**1. About perampanel (generic name: perampanel hydrate, product name: Fycompa®)**

Perampanel is a first-in-class AED discovered and developed by Eisai. With epileptic seizures being mediated by the neurotransmitter glutamate, the agent is a highly selective, noncompetitive AMPA receptor antagonist that reduces neuronal hyperexcitation associated with seizures by targeting glutamate activity at postsynaptic AMPA receptors. Perampanel is available in tablet form to be taken once daily orally at bedtime, and an oral suspension formulation has been approved in the United States and Europe.

The agent is currently approved in more than 50 countries and territories, including Japan, the United States and in Europe as an adjunctive treatment of partial-onset seizures (with or without secondarily generalized seizures) in adult and adolescent patients with epilepsy 12 years of age and older.

In addition, perampanel has been approved in more than 40 countries, including Japan, the United States and in Europe for the adjunctive therapy of primary generalized tonic-clonic (PGTC) seizures in patients with epilepsy 12 years of age and older. More specifically, Eisai has obtained approval for the agent indicated in the United States as an adjunctive treatment of PGTC seizures in patients with epilepsy 12 years of age and older, and in Europe as an adjunctive treatment of PGTC seizures in adult and adolescent patients from 12 years of age with idiopathic generalized epilepsy.

Perampanel is approved in Japan indicated as an adjunctive therapy for partial-onset seizures (including secondarily generalized seizures) or tonic-clonic seizures in patients with epilepsy showing inadequate response to other AEDs.

In addition, Eisai submitted a supplemental application for partial label change for perampanel as monotherapy for treatment of partial-onset seizures in patients with epilepsy 12 years of age and older based on new U.S. Food and Drug Administration policy.

For further information on Fycompa in the United States, including Important Safety Information, please visit the Fycompa product website (<https://www.fycompa.com>).

**2. About Study 311**

Study 311 is a global (United States, Europe, Japan, Asia) multicenter, open-label, single-arm trial with an extension phase to evaluate the safety, tolerability and exposure-efficacy relationship of perampanel oral suspension when administered as an adjunctive therapy in approximately 160 children (ages 4 to less than 12 years) with inadequately controlled partial-onset seizures or primary generalized tonic-clonic seizures.

Following the 23 week treatment phase in which patients are titrated to receive 2 – 16 mg of perampanel orally once-daily, long term safety will be assessed during an extension phase. In Japan, pediatric patients with partial-onset seizures will be titrated to receive 2 - 12 mg of perampanel orally once-daily.

### 3. About Study 338

Study 338 is a global (United States, Europe, Japan, Asia) double-blind, randomized, placebo-controlled trial with an open-label extension to demonstrate that perampanel, when given as adjunctive antiepileptic treatment, is superior to placebo in approximately 140 participants at least 2 years of age with inadequately-controlled seizures associated with LGS.

Patients will be titrated to receive up to 8 mg of perampanel orally once-daily. The study will compare the efficacy of perampanel and placebo in reducing incidence of seizures primarily associated with LGS (myoclonic, tonic, atonic seizures) during the treatment period of 18 weeks.

### 4. About Epilepsy

Epilepsy affects approximately 1 million people in Japan, 2.9 million people in the United States, 6 million people in Europe, and approximately 60 million people worldwide. As approximately 30% of patients with epilepsy are unable to control their seizures with currently available AEDs,<sup>1</sup> this is a disease with significant unmet medical need.

Epilepsy is broadly categorized by seizure type, with partial-onset seizures accounting for approximately 60% of epilepsy cases and generalized seizures accounting for approximately 40%. In a partial-onset seizure, an abnormal electrical disturbance occurs in a limited area of the brain, and sometimes may subsequently spread throughout the brain, becoming a generalized seizure (known as a secondarily generalized seizure). In a generalized seizure, abnormal electrical disturbances occur throughout the brain, and can be followed by a loss of consciousness or physical symptoms manifested throughout the whole body.

Accounting for approximately 60% of generalized epilepsy and approximately 20% of all epilepsy cases,<sup>2</sup> generalized tonic-clonic seizures are one of the most common and most severe forms of epileptic seizures as they can cause significant injury to patients from falling down suddenly, and the frequency of these seizures is the most important risk factor associated with sudden unexpected death in epilepsy (SUDEP).<sup>3</sup>

For the majority of patients, a generalized tonic-clonic seizure begins with a loss of consciousness without any prior warning symptoms and a sudden contraction of the tonic muscles, causing the patient to fall down (tonic phase). This is followed by violent convulsions (clonic phase) until the muscles finally relax, and the patient is left with a disturbance of consciousness. As this is a serious event, it is seen as a major hindrance on daily life. While the seizure generally only lasts a few minutes, the patient will often feel confused, groggy or drowsy for a short period of time before returning to normal.

### 5. About Lennox-Gastaut Syndrome

One of the most rare and severe forms of epilepsy, LGS usually develops in preschool-aged children, many of whom have some kind of preexisting organic brain disorder, such as encephalopathy. LGS is not only characterized by frequent seizures and multiple seizure types, it is also accompanied by delayed intellectual development and personality disorders. The majority of patients with LGS experience tonic (muscle stiffening), atonic (sudden loss of muscle tone or drop attacks) and absence (brief loss of consciousness or staring) seizures. Tonic-clonic (grand mal), myoclonic (sudden muscle jerks) and other types of seizures may also occur. Tonic and atonic seizures lead to the sudden falls seen in LGS patients that are known as “drop attacks,” a primary cause of injury. Patients with LGS often wear protective helmets with face guards to protect against head injury from these attacks. Although LGS is most commonly treated with AEDs, patients whose seizures are difficult to manage with pharmacotherapy may have to undergo surgical treatment.

<sup>1</sup> “The Epilepsies and Seizures: Hope Through Research. What are the epilepsies?” National Institute of Neurological Disorders and Stroke, accessed May 24, 2016, [http://www.ninds.nih.gov/disorders/epilepsy/detail\\_epilepsy.htm#230253109](http://www.ninds.nih.gov/disorders/epilepsy/detail_epilepsy.htm#230253109)

<sup>2</sup> Hauser WA, et al. *Epilepsia*, 34(3):453-468,1993

<sup>3</sup> Shorvon S, Tomson T. “Sudden unexpected death in epilepsy.” *Lancet*, 2011; 378:2028-2038