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Eisai Co., Ltd.

SUPPLEMENTARY NEW DRUG APPLICATION SUBMITTED IN JAPAN FOR FYCOMPA® AS MONOTHERAPY FOR PARTIAL-ONSET SEIZURES, PEDIATRIC INDICATION FOR PARTIAL-ONSET SEIZURES, AS WELL AS NEW FORMULATION

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has filed a supplementary new drug application in Japan for its in-house discovered antiepileptic drug (AED) Fycompa® (perampanel) seeking approval for use as monotherapy for partial-onset seizures, treatment for partial-onset seizures in pediatric patients aged 4 years and older, as well as a new fine granule formulation.

The submission covering monotherapy for partial-onset seizures was based on the results of a Phase III clinical study (FREEDOM/Study 342) conducted in Japan and South Korea. In FREEDOM, the percentage of untreated patients from 12 to 74 years of age with partial onset seizures who achieved seizure freedom with Fycompa monotherapy exceeded the criteria for efficacy*, and the primary endpoint was met. The most common adverse events (incidence of 10% or higher) observed in this study were dizziness, somnolence, nasopharyngitis and headache, which is consistent with the safety profile of Fycompa to date.

The submission covering partial-onset seizures in pediatric patients was based on the results of a Phase III clinical study (Study 311) of Fycompa as adjunctive therapy in pediatric patients conducted in Japan, the United States and Europe. In Study 311 which evaluated Fycompa in pediatric patients (ages 4 to less than 12 years) with inadequately controlled partial-onset seizures or primary generalized tonic-clonic seizures, it was demonstrated that the safety and efficacy of Fycompa in pediatric patients was similar to that observed in patients 12 years of age and older.

In addition, regarding the additional application for the fine granule formulation, Eisai developed this formulation to make it easier to administer Fycompa to children and patients who have difficulty taking tablets, and subsequently conducted a clinical study verifying bioequivalence with the tablet formulation, which led to this application.
Detailed results of FREEDOM and Study 311 will be presented at upcoming academic conferences.

Discovered at Eisai's Tsukuba Research Laboratories, Fycompa is a first-in-class AED that is a highly selective, noncompetitive AMPA receptor antagonist which reduces neuronal hyperexcitation by targeting glutamate activity at AMPA receptors on postsynaptic membranes. Available in tablet form to be taken orally once daily, Fycompa is approved in Japan as an adjunctive therapy for partial-onset seizures (including secondarily generalized seizures) or primary generalized tonic-clonic seizures in patients with epilepsy showing inadequate response to other AEDs.

It is estimated that there are approximately 1 million patients with epilepsy in Japan, and although onset occurs at any age, onset is most common in people aged 18 and younger and the elderly.

Eisai considers neurology including epilepsy, a therapeutic area of focus, and in continued pursuit of our mission to provide "seizure freedom" to a greater number of patients living with epilepsy. Eisai seeks to address the diverse needs of, as well as increasing the benefits provided to, patients with epilepsy and their families.

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[Notes to editors]

1. About Fycompa (perampanel)

Fycompa 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 AMPA receptors on postsynaptic membranes. Fycompa is available in tablet form to be taken once daily orally at bedtime. In addition, an oral suspension formulation has been approved in the United States.

Fycompa is currently approved in more than 55 countries and territories, including the United States, Japan, in Europe and in Asia as adjunctive treatment for partial-onset seizures (with or without secondarily generalized seizures) in patients with epilepsy 12 years of age and older. An application seeking approval for use in the adjunctive treatment of partial-onset seizures is under review in China, which has been designated for Priority Review. In addition, Fycompa has been approved in more than 50 countries, including the United States, Japan, in Europe and in Asia for treatment as an adjunctive therapy for primary generalized tonic-clonic seizures in patients with epilepsy 12 years of age and older. In the United States, Fycompa is approved for monotherapy and adjunctive use in the treatment of partial-onset seizures (with or without secondarily generalized seizures) in patients with epilepsy 4 years of age and older.

To date, Fycompa has been used to treat more than 200,000 patients worldwide across all indications.

Furthermore, Eisai is conducting a global Phase III clinical study (Study 338) for the agent in patients with seizures associated with Lennox-Gastaut syndrome.

2. About Study 342 (FREEDOM)

Study title:	An Uncontrolled, Open-label Study for Verification of Efficacy and Safety for Perampanel Monotherapy in Untreated Patients with Partial Onset Seizures (Including Secondarily Generalized Seizures)
Study population:	89 untreated patients aged 12 to 74 with partial-onset seizures with or without secondarily generalized seizures
Treatment administered:	Up to 4 mg of perampanel administered orally once daily before bedtime (may be titrated up to 8 mg if seizures occur)
Duration of treatment:	Treatment Phase (Titration Period: 6 weeks, Maintenance Period: 26 weeks (if titrated up from 4 mg to 8 mg, titration period is 4 weeks and treatment period is 26 weeks)) Extension Phase
Study locations:	Japan, South Korea
Primary endpoint:	Seizure-free rate during 26-week Maintenance Period for participants with partial onset seizures
Results:	89 patients were administered Fycompa as monotherapy, and the proportion of 73 patients for evaluation receiving 4 mg who were seizure-free during the treatment period exceeded the efficacy criteria*, and the primary endpoint was met. In addition, the interim results demonstrated that the 4 mg and 8 mg patients combined also exceeded the efficacy criteria. The most common adverse events (incidence of 10% or higher) observed in this study were dizziness, somnolence, nasopharyngitis and headache, which is consistent with the safety profile of Fycompa to date *The criteria for efficacy in this study with 73 patients for evaluation of efficacy required a 52.1% or higher proportion of patients to have achieved seizure freedom, which was set primarily in consideration of the results from other AED monotherapy studies.

3. About Study 311

Study title:	An Open-Label Study to Evaluate the Safety, Tolerability, and Exposure-Efficacy Relationship of Perampanel Oral Suspension When Administered as an Adjunctive Therapy in Pediatric Subjects With Inadequately Controlled Partial-Onset Seizures or Primary Generalized Tonic Clonic Seizures
Study population:	180 patients aged 4 to 12 with inadequately controlled partial-onset seizures or primarily generalized tonic-clonic seizures.
Treatment administered:	2 – 16 mg of perampanel administered orally once daily before bedtime
Duration of treatment:	Treatment Phase (Titration Period: up to 11 weeks, Maintenance Period: up to 12 weeks) Extension Phase
Study locations:	Global (United States, Europe, Japan, Asia)
Primary endpoint:	Safety and tolerability
Results:	In the 180 patients who were administered Fycompa, efficacy was similar to that observed in patients 12 years of age and older. The most common adverse events (incidence of 10% or higher) observed in this study were somnolence, nasopharyngitis, pyrexia, vomiting, dizziness, influenza, and irritability, which is consistent with the safety profile of Fycompa to date.

4. About Epilepsy

Epilepsy affects approximately 3.4 million people in the United States, 1 million people in Japan, 6 million people in Europe, 9 million people in China, and approximately 60 million people worldwide. As approximately 30% of patients with epilepsy are unable to control their seizures with currently available AEDs,[1] 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 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.

[1] "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