EISAI SUBMITS NEW DRUG APPLICATION IN JAPAN FOR IN-HOUSE-DISCOVERED ANTIEPILEPTIC DRUG PERAMPANEL AS ADJUNCTIVE THERAPY FOR PARTIAL-ONSET AND GENERALIZED TONIC-CLONIC SEIZURES

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, “Eisai”) announced today it has submitted a new drug application in Japan for its in-house-discovered antiepileptic drug (AED) perampanel hydrate (generic name, U.S. and Europe brand name: Fycompa®, “perampanel”) as an adjunctive therapy for partial-onset and primary generalized tonic-clonic seizures.

This submission utilizes the Pharmaceutical and Medica

accounting for approximately 40%. Primary generalized tonic-clonic seizures are one of the most common and most severe forms of generalized seizures, accounting for approximately 60% of generalized epilepsy and approximately 20% of all epilepsy cases.[2]

As approximately 30% of patients with epilepsy are unable to control their seizures with currently available AEDs,[3] this is a disease with significant unmet medical needs. The generalized tonic-clonic seizures that are covered in the indication for this application are one of the 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).[4] Eisai considers epilepsy a therapeutic area of focus and by providing multiple treatment options in addition to perampanel as part of an extensive epilepsy product portfolio, Eisai seeks to make continued contributions 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 perampanel hydrate (generic name, U.S. and Europe brand name: Fycompa, "perampanel")

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.

The agent is currently approved in more than 45 countries and territories, including Europe and the United States, as an adjunctive treatment (available as a once-daily oral dose) of partial-onset seizures (with or without secondarily generalized seizures) in adult and adolescent patients from 12 years of age with epilepsy, and has been launched in over 25 countries.

Applications seeking an additional indication for the adjunctive treatment of primary generalized tonic-clonic (PGTC) seizures in adult and adolescent patients from 12 years of age with generalized epilepsy were filed with regulatory authorities in Europe and the United States in August 2014, and approved in the United States and Europe in June 2015.

Eisai has submitted this regulatory application covering both PGTC seizures and partial-onset seizures based primarily on Study 332 and Study 335 in Japan.

Meanwhile, Eisai has submitted applications for the approval of an additional oral suspension formulation of perampanel in Europe and the United States in June 2015, and is conducting Phase II studies in Europe and the United States for partial-onset epilepsy in pediatric patients.

2. About Study 335

Study title:	A Multicenter, Double-blind, Randomized, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of Perampanel Administered as an Adjunctive Therapy in Subjects with Refractory Partial-onset Seizures
Study population:	710 patients aged 12 years and older who have a diagnosis of epilepsy with partial-onset seizures with or without secondarily generalized seizures receiving one to a maximum of three anti-epileptic drugs

Treatment administered:	Perampanel oral tablets, 4 mg/day, 8 mg/day and 12 mg/day, once daily before bedtime Perampanel-matched placebo oral tablets, once daily before bedtime
Duration of treatment:	Prerandomization Phase: 6 weeks Randomization Phase (treatment): 19 weeks (Titration Period, 6 weeks; Maintenance Period, 13 weeks) Extension Phase: over 10 weeks
Study locations:	Japan, China, South Korea, Australia, Thailand, Malaysia, Taiwan
Primary endpoint:	Percent change in seizure frequency per 28 days during treatment relative to baseline
Results:	Perampanel demonstrated a statistically significant reduction in seizure frequency at doses of 8 mg/day and 12 mg/day, compared to placebo
Adverse events:	The most common adverse events (>10% in the perampanel arms and greater than placebo) were dizziness and somnolence.

(Detailed results of the study will be presented at an academic conference in the near future.)

3. About Study 332[1]

Study title:	A Multicenter, Double-blind, Randomized, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of Adjunctive Perampanel in PGTC Seizures
Study population:	164 patients aged 12 years and older with PGTC seizures receiving one to a maximum of three anti-epileptic drugs
Treatment administered:	(Placebo-controlled) Perampanel oral tablets, once daily, up to 8 mg/day (Titration Period), randomized dose 8 mg/day (Maintenance Period)
Duration of treatment:	Prerandomization Phase (Screening and Baseline Periods): up to 12 weeks Randomization Phase (treatment): 17 weeks (Titration Period, 4 weeks; Maintenance Period, 13 weeks) Extension Phase: over 38 weeks
Study locations:	U.S., Europe, Japan, Asia
Primary endpoint:	Percent change in PGTC seizure frequency (percent change from baseline in PGTC seizure frequency per 28 days during treatment)
Results:	-A reduction in PGTC seizure frequency of 76.5% was observed for perampanel, which was statistically significant when compared to a reduction of 38.4% for placebo ($p<0.0001$). -The responder rate for perampanel was 64.2%, which was a statistically significant improvement over the responder rate (percentage of patients who experience a 50% or greater reduction in PGTC seizure frequency per 28 days in the Maintenance period relative to baseline) for placebo of 39.5% ($p=0.0019$). -For patients who had been unable to adequately control PGTC seizures with existing

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,[3] this is a disease with significant unmet medical needs.

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 seco