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Eisai Co., Ltd.

EISAI RECEIVES POSITIVE CHMP OPINION ON INDICATION EXPANSION FOR ANTIEPILEPTIC AGENT FYCOMPA® (PERAMPANEL) AS ADJUNCTIVE TREATMENT OF PRIMARY GENERALIZED TONIC-CLONIC SEIZURES

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that its U.K. subsidiary Eisai Europe Ltd. has received a positive opinion from the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) for the use of Fycompa® (perampanel) for the adjunctive treatment of primary generalized tonic-clonic (PGTC) seizures in adult and adolescent patients from 12 years of age with idiopathic generalized epilepsy.

PGTC 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.[1] The CHMP based its opinion on a multicenter, double-blind, randomized, placebo-controlled, parallel-group study (Study 332) to evaluate the efficacy and safety of adjunctive Fycompa therapy in 164 patients aged 12 years and older with PGTC seizures receiving one to a maximum of three anti-epileptic drugs.[2] As one of the primary endpoints of the study, the responder rate for Fycompa was 64.2%, which was a statistically significant improvement over the responder rate for placebo of 39.5% ($p=0.0019$). Additionally, a reduction in PGTC seizure frequency of 76.5% was observed in the Fycompa group, which was statistically significant when compared to a reduction of 38.4% for placebo ($p<0.0001$). Furthermore, 30.9% of patients treated with Fycompa were free of PGTC seizures (12.3% for placebo) during the 13 week maintenance period. The most common adverse events for Fycompa and placebo were, respectively, dizziness, fatigue, headache, somnolence and irritability.

Fycompa is a first-in-class AED discovered and developed by Eisai. 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.

Epilepsy affects nearly 2.4 million people in Europe (G5). Fycompa was launched in Europe as an adjunctive treatment for partial-onset seizures (with or without secondary generalized seizures) in patients with epilepsy aged 12 years and older in September 2012. Currently the agent is approved for this indication in over 45 countries, and has been launched in over 25 countries.

Eisai considers epilepsy a therapeutic area of focus and by providing multiple treatment options in addition to Fycompa 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 Fycompa (perampanel)

Fycompa is a first-in-class AED discovered and developed by Eisai. With epileptic seizures being primarily 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 (once-daily oral dose) of partial-onset seizures and has been launched in over 25 countries.

Applications seeking an additional indication for the adjunctive treatment of PGTC seizures in patients with epilepsy aged 12 years and older based on the results of this study were filed with regulatory authorities in Europe and the United States in August 2014. Applications are also under review in Switzerland and Russia.

A Phase III study of Fycompa in partial-onset seizures (Study 335) conducted in Asia, including Japan, met its primary endpoint. The company plans to submit a regulatory application covering both PGTC seizures and partial-onset seizures based on Study 332 and Study 335 in Japan during the first half of fiscal 2015. Furthermore, Eisai is conducting Phase II studies in Europe and the United States for partial-onset epilepsy in pediatric patients.

2. About Study 332

A Multicenter, Double-blind, Randomized, Placebo-controlled Study to Evaluate the Efficacy and Safety of Adjunctive Perampanel in Primary Generalized Tonic Clonic Seizures

Study population:	164 patients aged 12 years and older with PGTC seizures receiving one to a maximum of three anti-epileptic drugs
Primary objective:	To demonstrate the efficacy of adjunctive perampanel therapy, compared to placebo, on PGTC seizures
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 endpoints:	-Responder rate (EU): Percentage of patients who experience a 50% or greater reduction in PGTC seizure frequency per 28 days in the Maintenance period relative to baseline -Percent change in PGTC seizure frequency (U.S.): Percent change from baseline in PGTC seizure frequency per 28 days during treatment
Results:	-The responder rate for Fycompa was 64.2%, which was a statistically significant improvement over the responder rate for placebo of 39.5% (p=0.0019). -A reduction in PGTC seizure frequency of 76.5% was observed in the Fycompa group, which was statistically significant when compared to a reduction of 38.4% for placebo (p<0.0001). -For patients who had been unable to adequately control PGTC seizures with existing AEDs, 30.9% of patients treated with Fycompa were free of PGTC seizures (12.3% for placebo) during the 13 week Maintenance period.

Adverse events:	The most common adverse events (>10% in the Fycompa arm and greater than placebo) for Fycompa and placebo were, respectively, dizziness (32.1% vs 6.1%), fatigue (14.8% vs 6.1%), headache (12.3% vs 9.8%), somnolence (11.1% vs 3.7%) and irritability (11.1% vs 2.4%).

3. About Primary Generalized Tonic-Clonic Seizures

Epilepsy affects nearly 1 million people in Japan, 2.4 million people in Europe (G5: United Kingdom, France, Germany, Italy and Spain), 2.2 million people in the United States, and more than 50 million people worldwide. 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%. Primary generalized tonic-clonic (PGTC) 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.[1] For the majority of patients, a PGTC 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.

[1] Hauser WA, et al. Epilepsia, 34(3):453-468,1993

[2] French JA, et al. “Adjunctive Perampanel for Treatment of Drug-Resistant Primary Generalized Tonic-Clonic Seizures in Patients with Idiopathic Generalized Epilepsy: A Double-Blind, Randomized, Placebo-Controlled Phase III Trial.” Abstract. *68th American Epilepsy Society (AES) Annual Meeting*, 2014; 2.389