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Eisai Co., Ltd.

U.S. FDA APPROVES EISAI'S AMPA RECEPTOR ANTAGONIST FYCOMPA™ (PERAMPANEL) AS ADJUNCTIVE TREATMENT FOR PARTIAL-ONSET SEIZURES IN PATIENTS WITH EPILEPSY AGE 12 AND OLDER

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that its U.S. subsidiary Eisai Inc. has received approval from the U.S. Food and Drug Administration (FDA) for the AMPA receptor antagonist Fycompa™ (perampanel) as an adjunctive treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy age 12 years and older.

Discovered and developed by Eisai, Fycompa is a non-competitive AMPA-type glutamate receptor antagonist. As an AMPA receptor antagonist, Fycompa reduces neuronal hyperexcitation associated with seizures by inhibiting glutamate activity at post-synaptic AMPA receptors. This is the first antiepileptic agent approved by the U.S. FDA to work in this manner.

The approval decision was based primarily on clinical data from three pivotal Phase III, global, randomized, double-blind, placebo-controlled, dose-escalation studies that examined 1,480 patients with partial-onset seizures. These studies demonstrated that Fycompa, as an adjunctive therapy, significantly reduced seizure frequency in patients with partial-onset seizures with or without secondary generalized seizures. The most commonly reported adverse events were dizziness, somnolence, fatigue, irritability, falls, nausea, ataxia, balance disorder, gait disturbance, vertigo and weight gain. Serious or life-threatening psychiatric (mental) problems were also seen more frequently in patients treated with Fycompa. These reactions are described in the boxed warning bolded below.

The FDA has recommended that Fycompa be classified by the U.S. Drug Enforcement Administration (DEA) as a scheduled drug under the country's Controlled Substances Act. Once the DEA has provided the final scheduling designation, Eisai will announce when Fycompa will be available to patients and physicians in the United States.

There are an estimated 2.2 million people living with epilepsy in the United States, and more than 50 million people living with epilepsy worldwide. Eisai defines epilepsy as a therapeutic area of focus, with its currently marketed U.S. epilepsy portfolio comprising Zonegran® (under license from the originator, Dainippon Sumitomo Pharma Co., Ltd.) as an adjunctive treatment for adult epilepsy patients with partial-onset seizures, and Banzel® (under license from the originator, Novartis AG) for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome, a severe form of early childhood-onset epilepsy. By providing multiple treatment options as part of an abundant product portfolio in the field of antiepileptic drugs, Eisai seeks to make further contributions to address the diversified needs of, and increase the benefits provided to, epilepsy patients and their families.

[Please refer to the following notes for further information on epilepsy, Fycompa (perampanel), perampanel Phase III studies, and Eisai's Commitment to Epilepsy.]

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[Notes to editors]

1. About epilepsy

Epilepsy is a medical condition that produces seizures, affecting a variety of mental and physical functions. A patient is considered to have epilepsy after two or more unprovoked seizures. A seizure occurs when a brief, strong surge of electrical activity affects part or all of the brain. An individual can have various symptoms, from convulsions and loss of consciousness, to some that are not always recognized as seizures, such as blank staring, lip smacking, or jerking movements of arms and legs.

Epilepsy can develop at any age and 0.5% to 2% of people will develop epilepsy during their lifetime. Epilepsy reportedly affects nearly 1 million people in Japan, 2.4 million people in Europe (G5), 2.2 million people in the United States, and more than 50 million people worldwide. Epilepsy constitutes an area in which there are still significant unmet medical needs, with partial-onset epilepsy accounting for approximately 60% of all epilepsy cases in the United States, and from 25% to 30% of patients living with partial epilepsy in that country not achieving seizure freedom despite therapy with antiepileptic drugs.

2. About Fycompa (perampanel)

Fycompa (perampanel), a novel chemical entity discovered and developed by Eisai, is a non-competitive AMPA-type glutamate receptor antagonist. Fycompa is the first antiepileptic treatment to reduce neuronal hyperexcitation associated with seizures by targeting glutamate activity at post-synaptic AMPA receptors. Fycompa has demonstrated anti-seizure effects in Phase II and III studies. The agent is approved in Europe and the United States as a treatment (once-daily oral dose) of partial-onset seizures, and is also being evaluated in a Phase III study in Asia including Japan. Furthermore, Eisai is conducting a global Phase III perampanel study for generalized epilepsy and Phase II perampanel studies in Europe and the United States for partial-onset epilepsy in pediatric patients, as it seeks to expand the range of indications for which the drug is approved.

[Important Safety Information Summary in the United States]

Mental (Psychiatric) Problems

Fycompa may cause new or worse aggressive behavior (including homicidal behavior), hostility, anger, anxiety, or irritability, being suspicious or distrustful (believing things that are not true) or other unusual or extreme changes in behavior or mood. Patients should call their healthcare provider right away if they have any new or worsening mental problems while taking Fycompa.

Suicidal Thoughts and Actions

Antiepileptic drugs, including Fycompa, may cause suicidal thoughts or actions in a very small number of people, about 1 in 500. Patients should call their healthcare provider right away if they have any new or worsening symptoms of depression, any unusual or sudden changes in mood, feelings, behavior, or suicidal thoughts, behavior, or thoughts of self-harm that they have never had before or may be worse than before.

Dizziness, Vertigo (Sense of Spinning) and Problems Walking Normally

Patients may have problems walking normally if they are unsteady because they feel dizzy. These symptoms may increase when their dose of Fycompa is increased. A patient's risk of feeling dizzy and having problems walking normally may be higher if they are elderly.

Sleepiness and Tiredness

Fycompa may make a patient feel sleepy or tired. Patients should not drive, operate heavy machinery, or do other dangerous activities until they know how Fycompa affects them. A patient's risk of feeling sleepy and tired may be higher if they are elderly.

Falls

Taking Fycompa may increase a patient's chance of falling. These falls can cause serious injuries. A patient's risk of falling may be higher if they are elderly.

Withdrawal of AEDs

Patients must not stop Fycompa without first talking to their healthcare provider. Stopping Fycompa suddenly can cause serious problems and can cause patients to have seizures more often.

3. About Phase III studies for perampanel approval

The clinical development plan for perampanel consisted of three global Phase III studies (Studies 306, 305 and 304) in which a total of 1,480 epilepsy patients aged 12 years and older participated. The key goal of Study 306 was to identify the minimal effective dose and included four treatment arms (placebo, 2 mg, 4 mg, and 8 mg). Studies 304 and 305 included three arms (placebo, 8 mg, and 12 mg) and were to evaluate a more extended dose range.

The studies were similar in design: global, randomized, double-blind, placebo-controlled, dose-escalation, parallel-group studies. The primary and secondary endpoints were the same in all the studies: percentage change in seizure frequency, 50% responder rate, percentage reduction of complex partial plus secondarily generalized seizures, and evaluation for dose response. The primary endpoint for the European Medicines Agency (EMA) were the 50% responder rates, while for the U.S. FDA it was the median percentage changes in seizure frequency. Specifically, the results showed:

<u>Study 306</u>

·The 50% responder rates compared to placebo for the ITT (intention-to-treat) population were: 20.6% (p=0.4863), 28.5% (p=0.0132), and 34.9% (p=0.0003) in the 2, 4, and 8 mg perampanel/day groups, respectively, versus 17.9% with placebo.

·The median percentage changes in seizure frequency for the ITT population shown were: 2 mg = -13.6% (p=0.4197), 4 mg = -23.3% (p=0.0026), 8 mg = -30.8% (p<0.0001), and placebo = -10.7%.

·The most frequent treatment-emergent adverse events were dizziness, headache and somnolence.

<u>Study 305</u>

·The 50% responder rates compared to placebo for the ITT (intention-to-treat) population were: 33.3% (p=0.0018) and 33.9% (p=0.0006) in the 8 mg and 12 mg perampanel/day groups, respectively, versus 14.7% with placebo.

·The median percentage changes in seizure frequency for the ITT population shown were: 8mg = -30.5% (p=0.0008), 12mg = -17.6% (p=0.0105), and placebo = -9.7%.

·The most reported adverse events were dizziness, fatigue, headache and somnolence.

<u>Study 304</u>

·The 50% responder rates compared to placebo for the ITT (intention-to-treat) population were: 37.6% (p=0.0760) and 36.1% (p=0.0914) in the 8 mg and 12 mg perampanel/day groups, respectively, versus 26.4% with placebo.

·The median percentage changes in seizure frequency for the ITT population shown were: 8mg = -26.3% (p=0.0261), 12mg = -34.5% (p=0.0158), and placebo = -21.0%.

·The most common side effects were dizziness, somnolence, irritability, headache, falls and ataxia.

4. Eisai's Commitment to Epilepsy

Eisai defines epilepsy as a therapeutic area of focus. In addition to developing the AMPA receptor antagonist perampanel globally, it currently markets Zonegran® (sodium/calcium channel-blocking antiepileptic agent under

license from the originator Dainippon Sumitomo Pharma Co., Ltd. and marketed in Europe, the United States and Asia) and Zebinix® (voltage-dependent sodium channel-blocking antiepileptic agent under license from the originator BIAL-Portela & Ca S.A. and marketed in Europe), both as adjunctive treatments in adults with partial-onset seizures; Inovelon®/Banzel® (sodium channel-blocking novel triazole-derived antiepileptic agent under license from the originator Novartis AG and marketed in Europe, Asia [Inovelon®] and North America [Banzel®]) for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome, which is a severe form of early childhood-onset epilepsy; and Fostoin® (water-soluble phenytoin prodrug co-promoted with Nobelpharma Co., Ltd. and marketed in Japan), which is an anticonvulsant agent used to treat status epilepticus and other such conditions.