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New Drug Application for Insomnia Disorder Treatment Lemborexant Submitted in the United States

TOKYO and STAMFORD, Conn. – January 15, 2019 – Eisai Co., Ltd. (CEO: Haruo Naito, "Eisai") and Purdue Pharma L.P. (President and CEO: Craig Landau, MD, "Purdue Pharma") today announced that a new drug application has been submitted to the U.S. Food and Drug Administration (FDA) for lemborexant, an investigational agent for sleep-wake regulation, seeking approval for the treatment of insomnia, a sleep-wake disorder.

This application was based on the results of two pivotal Phase 3 clinical studies in patients with insomnia, SUNRISE 1 (Study 304) and SUNRISE 2 (Study 303), enrolling approximately 2,000 patients, as well as important safety studies, including assessment of postural stability after middle-of-the-night awakening and a next-morning driving study. SUNRISE 1, a one-month, double-blind, placebo-controlled study, included the first ever Phase 3 head-to-head comparison versus zolpidem ER and objectively assessed sleep parameters (time to sleep onset, sleep efficiency, and wake after sleep onset) resulting in the largest (objective) polysomnography dataset collected to date in patients with insomnia. SUNRISE 2 was a 12-month study and subjectively assessed for ability to fall asleep and stay asleep based on patient self reports (sleep diaries).

Lemborexant, which acts on the orexin neurotransmitter system and is believed to regulate sleep and wake by dampening wakefulness without impeding the ability to awaken to external stimuli, is being jointly developed by Eisai and Purdue Pharma for the treatment of multiple sleep-wake disorders, including insomnia disorder. In addition to the treatment of insomnia disorder, a Phase 2 clinical study of lemborexant in patients with irregular sleep-wake rhythm disorder and mild to moderate Alzheimer's dementia is underway. Information about ongoing clinical studies is available at clinicaltrials.gov.

Eisai and Purdue Pharma are striving to address new unmet medical needs and to improve the lives of patients and their families.

This release discusses investigational uses of an agent in development and is not intended to convey conclusions about efficacy or safety. There is no guarantee that such an investigational agent will successfully complete clinical development or gain health authority approval.

<Notes to editors>

1. About Lemborexant

Lemborexant is a novel investigational small molecule compound, discovered and developed by Eisai in-house scientists, that inhibits orexin signaling by binding competitively to both orexin receptor subtypes (orexin receptor 1 and 2). In individuals with normal daily sleep-wake rhythms, orexin signaling is believed to promote periods of wakefulness. In individuals with sleep-wake disorders, it is possible that orexin signaling which regulates wakefulness is not functioning normally, suggesting that inhibiting inappropriate orexin signaling may enable initiation and maintenance of sleep.

2. About SUNRISE 1 (Study 304)[1]

SUNRISE 1 was a multicenter, randomized, double-blind, placebo-controlled, active comparator, parallel-group study evaluating the efficacy and safety of lemborexant in 1,006 male or female adult patients 55 years and older (45 percent of patients were 65 years and older) with insomnia disorder conducted in North America and Europe. SUNRISE 1 included a pre-randomization phase of up to 35 days (including a two-week placebo run-in period) and a randomization phase comprised of a 30-day treatment period and a minimum two-week period without treatment prior to the end-of-study visit. In this study, patients were randomized to receive placebo or one of three treatment regimens (lemborexant 5 mg, lemborexant 10 mg, zolpidem ER 6.25 mg). The primary objective for SUNRISE 1 was to demonstrate using polysomnography that lemborexant at either the 5 mg or 10 mg dose is superior to placebo on objective sleep onset, as measured by latency to persistent sleep after the last two nights of one month of treatment. Key secondary objectives included change from baseline in sleep efficiency and wake after sleep onset (WASO) for both lemborexant doses compared to placebo, and WASO in the second half of the night (WASO2H) for both lemborexant doses compared to zolpidem ER, each after the last two nights of one month of treatment.

3. About SUNRISE 2 (Study 303)[2]

SUNRISE 2 was a 12-month multicenter, global, randomized, controlled, double-blind, parallel-group study of the efficacy and safety of lemborexant in 949 male or female adult participants 18 to 88 years of age with insomnia disorder. SUNRISE 2 included a pre-randomization phase of up to 35 days (including a two-week placebo run-in period) and a randomization phase comprised of a six-month placebo-controlled treatment period, a six-month period of only active treatment and a two-week period without treatment prior to the end-of-study-visit. In this study, during the placebo-controlled treatment period, patients were randomized to receive placebo or one of two treatment regimens (lemborexant 5 mg or 10 mg). During the active-only treatment period, patients who received placebo during the first period were re-randomized to receive lemborexant 5 mg or 10 mg. Patients who received active treatment during the first period continued on the treatment to which they were originally randomized. The primary objective was to determine the efficacy of lemborexant 5 mg and 10 mg compared to placebo on patient-reported (subjective) sleep onset latency after six months of treatment. Key secondary endpoints were mean change from baseline in subjective sleep efficiency and subjective wake after sleep onset (sWASO) for lemborexant 5 mg and 10 mg compared to placebo after six months of treatment.

4. About Sleep Disorders

Population studies show that sleep disorders affect many more people worldwide than previously thought.[3] Insomnia disorder is the most common sleep disorder affecting approximately 30 percent

of the adult population worldwide.[3,4] Insomnia disorder is characterized by difficulty falling asleep, staying asleep or both, despite an adequate opportunity to sleep, which can lead to daytime consequences such as fatigue, difficulty concentrating and irritability.[5,6]

Sleeping well is essential for good health, including brain health. Poor sleep is associated with a wide range of health consequences, including an increased risk of hypertension, accidental injury, diabetes, obesity, depression, heart attack, stroke and dementia, as well as adverse effects on mood and behavior.[5,7]

Experimental studies in animals and humans provide evidence of associations between sleep and disease risk factors, diseases and mortality.[8] Studies suggest an optimal sleep duration between seven and eight hours.[9]

Women are 1.4 times more likely than men to suffer from insomnia.[10] Older adults also have higher prevalence of insomnia; aging is often accompanied by changes in sleep patterns, including disrupted sleep, frequent waking and early waking, that can lead to less sleep time.[11]

5. About Eisai Co., Ltd

Eisai Co., Ltd. is a leading global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our *human health care* (*hhc*) philosophy. With over 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our *hhc* philosophy by delivering innovative products in various therapeutic areas with high unmet medical needs, including Neurology and Oncology.

Furthermore, we invest and participate in several partnership-based initiatives to improve access to medicines in developing and emerging countries.

For more information about Eisai Co., Ltd., please visit www.eisai.com.

6. About Purdue Pharma L.P.

Purdue Pharma L.P. develops and provides prescription medicines that meet the evolving needs of healthcare professionals, patients, and caregivers. We were founded by physicians and we are currently led by a physician. Beyond our efforts to provide quality medications, Purdue Pharma is committed to supporting national, regional and local collaborations to drive innovations in patient care. Privately held, Purdue Pharma is pursuing a pipeline of new medications and technologies through internal research & development and strategic industry partnerships. For more information, please visit www.purduepharma.com.

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