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**Eisai and Purdue Pharma Present Efficacy and Safety Data from
Second Pivotal Phase 3 Study at the Sleep Research Society's Conference:
Advances in Sleep and Circadian Science**

**Six-month data show significant improvements in patient-reported measures of sleep onset and
sleep maintenance for investigational agent lemborexant**

TOKYO and STAMFORD, Conn. – February 4, 2019 – Eisai Co., Ltd. (CEO: Haruo Naito, “Eisai”) and Purdue Pharma L.P. (President and CEO: Craig Landau, MD, “Purdue Pharma”) today announced six-month results from SUNRISE 2, a long-term Phase 3 clinical study evaluating the efficacy and safety of lemborexant, an investigational agent being developed for the treatment of insomnia, a sleep-wake disorder. Data were presented at the Sleep Research Society's Advances in Sleep and Circadian Science conference, taking place in Clearwater Beach, Florida, Feb. 1-4, 2019.

SUNRISE 2 was a 12-month multicenter, global, randomized, controlled, double-blind, parallel-group study of the efficacy and safety of lemborexant in 949 adult patients (18 to 88 years of age) with insomnia disorder, which was characterized by difficulty falling asleep and/or staying asleep. Approximately 28 percent of the patients randomized and treated were 65 years of age or older. During the first six months of the study, patients were randomized to receive either lemborexant 5 mg, lemborexant 10 mg, or placebo. The primary and key secondary efficacy objectives were assessed by patient self-reports via electronic sleep diaries.

At the end of the six-month, placebo-controlled treatment period, treatment with lemborexant at either 5 mg or 10 mg resulted in statistically significant improvements compared to placebo in patient-reported (subjective) sleep onset latency (sSOL), the study's primary efficacy endpoint, and subjective sleep efficiency (sSE) and subjective wake after sleep onset (sWASO), the study's key secondary endpoints. Six-month results from the study showed that:

- Median reductions from baseline in sSOL with lemborexant 5 mg (–21.81 minutes) and 10 mg (–28.21 minutes) were larger and statistically significant compared to placebo (–11.43 minutes) at the end of month six ($p < 0.0001$ for all treatment groups).
- Improvements from baseline, as measured by Least Squares Mean (LSM), in sSE with lemborexant 5 mg (14.19 percent, $p = 0.0001$) and 10 mg (14.31 percent, $p < 0.0001$) were larger and statistically significant compared to placebo (9.64 percent) at the end of month six.
- Reductions from baseline in sWASO, as measured by LSM, with lemborexant 5 mg (–46.75 minutes, $p = 0.0005$) and 10 mg (–41.95 minutes, $p = 0.0105$) were larger and statistically significant compared with placebo (–29.28 minutes) at the end of month six.

Most adverse events (AEs) reported were mild to moderate. Serious AEs were reported at a rate of 2.2 percent (lemborexant 5 mg), and 2.9 percent (lemborexant 10 mg), and 1.6 percent (placebo); only one was

considered treatment-related. The most common AEs reported, greater than 5 percent in either lemborexant treatment arm and greater than placebo, were somnolence, headache, and influenza. Discontinuation rates due to AEs were comparable between placebo and lemborexant 5 mg (3.8 percent and 4.1 percent, respectively), and higher for lemborexant 10 mg (8.3 percent).

“These findings add to the growing body of clinical data supporting the development of lemborexant for the treatment of insomnia, and we look forward to presenting 12-month results from the study in a future scientific forum,” said Lynn Kramer, MD, Chief Clinical Officer and Chief Medical Officer, Neurology Business Group, Eisai. “It remains our aspiration to bring a medicine to physicians and patients that helps patients sleep well at night and wake well in the morning.”

SUNRISE 2 is one of two Phase 3 safety and efficacy studies of lemborexant conducted by Eisai and Purdue Pharma. These studies supported the New Drug Application for lemborexant for the treatment of insomnia, filed with the U.S. Food and Drug Administration, on December 27, 2018. In Japan, an application is scheduled to be filed within fiscal 2018.

“The six-month findings from SUNRISE 2 are exciting, highlighting improvements in subjective measures of both sleep onset and sleep maintenance,” said John Renger, PhD, Head of Research & Development and Regulatory Affairs, Purdue Pharma. “SUNRISE 2 was a robust Phase 3 clinical study in which the self-reported patient outcomes are encouraging as they reflect the patients’ perception of lemborexant’s impact on enabling the patient to both fall asleep faster and stay asleep longer.”

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 2¹

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 active-only 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 at the end of 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 at the end of six months of treatment.

3. About Sleep Disorders

Population studies show that sleep disorders affect many more people worldwide than previously thought.² Insomnia disorder is the most common sleep disorder affecting approximately 30 percent of the adult population worldwide.^{2,3} 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.^{4,5}

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.^{4,6}

Experimental studies in animals and humans provide evidence of associations between sleep and disease risk factors, diseases and mortality.⁷ Studies suggest an optimal sleep duration between seven and eight hours.⁸

Women are 1.4 times more likely than men to suffer from insomnia.⁹ 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.¹⁰

4. 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 approximately 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 <https://www.eisai.com>.

5. 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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