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Eisai and Purdue Pharma Announce Positive Topline Results of SUNRISE 2, the Second Phase 3 Pivotal Study of Lemborexant

Long-term efficacy and safety evaluation in patients with insomnia, a sleep-wake disorder, met primary and key secondary efficacy objectives

TOKYO and STAMFORD, Conn. – October 17, 2018 – Eisai Co., Ltd. (CEO: Haruo Naito, "Eisai") and Purdue Pharma L.P. (President and CEO: Craig Landau, "Purdue Pharma") today announced positive topline results from SUNRISE 2, a long-term Phase 3 efficacy and safety evaluation of lemborexant, an investigational agent for sleep-wake regulation currently being studied for the potential treatment of multiple sleep-wake disorders. Topline results reported today are the primary and key secondary outcomes of the study from the six-month, placebo-controlled treatment period; the study is ongoing to 12 months. Eisai and Purdue Pharma plan to present full results from SUNRISE 2 at upcoming medical meetings in 2019.

SUNRISE 2 enrolled more than 900 adult patients (18 to 88 years of age) with insomnia disorder, characterized by difficulty falling asleep and/or staying asleep. The study met the pre-specified primary and key secondary efficacy objectives assessed by patient self-reports (sleep diaries). At the end of the six-month, placebo-controlled treatment period, lemborexant 5 mg and 10 mg provided statistically significant improvement in subjective sleep onset latency compared to placebo, the study's primary endpoint. Lemborexant 5 mg and 10 mg also provided statistically significant improvement in sleep maintenance variables of subjective sleep efficiency and subjective wake after sleep onset compared to placebo, which were the study's key secondary endpoints. Daily functioning, as measured by the Insomnia Severity Index, was also improved by both lemborexant 5 mg and 10 mg compared to placebo. The most common adverse events (AEs), greater than 5 percent in either lemborexant treatment arm and greater than placebo, were somnolence, headache, and influenza. Overall discontinuation rates due to AEs were comparable between placebo and lemborexant 5 mg, and higher for lemborexant 10 mg.

"As a clinician and researcher treating patients with insomnia and other sleep-wake disorders for 30 years, for me, successful treatment means that patients fall asleep fast, sleep well, and wake well, without functional impairment, or loss of effect over time," said Russell Rosenberg, PhD, D.ABSM, a Principal Investigator in the lemborexant studies and former Chairman of the Board of the National Sleep Foundation. "The results of SUNRISE 2 are particularly encouraging for the many patients who suffer from chronic insomnia."

The results of SUNRISE 2 build on a growing body of knowledge supporting the development of lemborexant, including SUNRISE 1, a recently completed Phase 3 study of lemborexant 5 mg and 10 mg versus placebo, including a superiority comparison to zolpidem tartrate extended release (zolpidem ER) as a secondary endpoint, as well as key safety studies evaluating for impairment as assessed by the ability to maintain postural stability – a predictor of risk for falls – after middle-of-the-night and next morning awakening and next-morning driving performance.

“Our aspiration for lemborexant is to bring to the millions of patients suffering from insomnia and other sleep-wake disorders an agent for sleep-wake regulation that improves their ability to fall asleep and stay asleep, and maintains efficacy over time,” said Lynn Kramer, MD, Chief Clinical Officer and Chief Medical Officer, Neurology Business Group, Eisai. “In SUNRISE 2, lemborexant improved time to sleep onset and sleep maintenance over a six-month period. With these results, we now look forward to proceeding with regulatory submissions for lemborexant to bring to patients a long-term treatment option for treating the sleep-wake disorder, insomnia.”

Lemborexant 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.

“We understand the importance of sleep-wake regulation to overall health and patient outcomes and, alongside our collaboration partner, Eisai, look forward to continued research as part of our commitment to a variety of patient populations with sleep-wake disorders,” said Marcelo Bigal, MD, PhD, Chief Medical Officer, Purdue Pharma.

Discovered by Eisai, lemborexant is being jointly developed by Eisai and Purdue Pharma. Information about ongoing clinical studies is available at clinicaltrials.gov.

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 investigational agent will successfully complete clinical development or gain health authority approval.

<Notes to editors>

1. About Lemborexant

Lemborexant, an investigational dual orexin receptor antagonist, is Eisai's in-house discovered and developed small molecule compound which inhibits orexin neurotransmission, or signaling, by binding competitively to two subtypes of orexin receptors (orexin receptor 1 and 2). In individuals with sleep-wake disorders, it is possible that the orexin system which regulates wakefulness is not functioning normally. During normal periods of sleep, orexin system activity is suppressed, suggesting it is possible to purposefully counteract inappropriate wakefulness and facilitate the initiation and maintenance of sleep.

Eisai and Purdue Pharma are investigating lemborexant as a potential treatment option for insomnia and other sleep-wake disorders. A Phase 2 clinical study of lemborexant in patients with irregular sleep-wake rhythm disorder and mild to moderate Alzheimer's dementia is underway.

2. About SUNRISE 2 / Study 303[1]

A 12-month multicenter, global, randomized, controlled, double-blind, parallel group study of 971 male or female adult participants (18 to 88 years of age) with insomnia disorder, including a screening and two-week placebo run-in period, a 52-week treatment period and a two-week follow-up period. All patients received lemborexant for at least six months during the study. Lemborexant 5 mg, 10 mg or matching placebo was taken orally in tablet form at home each night immediately before the patient intended to try to sleep for the first six months of study. The primary outcome measure was mean change from baseline in subjective sleep onset latency after six months of placebo-controlled treatment. Key secondary outcome measures were mean change from baseline in subjective sleep efficiency and subjective wake after sleep onset after six months of placebo-controlled treatment.

3. About Sleep Disorders

Population studies show that sleep disorders affect many more people worldwide than previously thought.[2] Insomnia disorder is characterized by difficulty falling sleep, staying asleep or both, despite an adequate opportunity to sleep, that can lead to daytime consequences such as fatigue, difficulty concentrating and irritability.[3,4] Insomnia disorder is the most common sleep disorder, with persistent insomnia symptoms experienced by approximately 10 percent of the adult population.[2,3] 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.[4,5]

Experimental studies in animals and humans provide evidence of associations between sleep and disease risk factors, diseases and mortality.[2,6] Studies suggest an optimal sleep duration between seven and eight hours.[2,6] Women are 1.4 times more likely than men to suffer from insomnia.[7]

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.[8]

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 to address unmet medical needs, with a particular focus in our strategic areas of Oncology and Neurology.

As a global pharmaceutical company, our mission extends to patients around the world through our investment and participation in 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/.

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 is committed to supporting national, regional and local collaborations to drive innovations in patient care. Privately held, Purdue 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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