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Eisai Co., Ltd.

EISAI PRESENTS NEW DATA ON LEMBOREXANT FOR TREATMENT OF IRREGULAR SLEEP-WAKE RHYTHM DISORDER IN PATIENTS WITH ALZHEIMER'S DISEASE AT THE 11TH CLINICAL TRIALS IN ALZHEIMER'S DISEASE CONFERENCE

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced that Eisai presented new data from Study 202, a Phase II evaluation of lemborexant, an investigational sleep-wake regulation agent, for the treatment of Irregular Sleep-Wake Rhythm Disorder (ISWRD) in patients with mild to moderate Alzheimer's disease. The data were presented at the 11th Clinical Trials in Alzheimer's Disease (CTAD) Conference in Barcelona, Spain. Lemborexant is being developed for the treatment of multiple sleep-wake disorders, including insomnia disorder.

ISWRD is a type of circadian rhythm sleep disorder where the pattern of sleep and wakefulness that repeats itself over a 24-hour period in healthy individuals is broken down, and sleeping and waking occur instead at various times during the day and night. This is often observed in patients with neurodegenerative diseases such as Alzheimer's disease. There is no known treatment approved for an irregular sleep-wake pattern in patients, meaning this is a condition with high unmet medical need.

Study 202 was a global, multicenter, randomized, double-blind, placebo-controlled, parallel-group study of the efficacy and safety of lemborexant in 62 patients 64 to 89 years of age with ISWRD and mild to moderate Alzheimer's disease. The primary objective of this study was to provide proof of concept of lemborexant's effects on ISWRD by evaluating the change from baseline in circadian rhythm-related parameters, nighttime sleep-related parameters and daytime wake-related parameters using actigraphy over four weeks of treatment. An actigraph is a non-invasive device worn on the wrist that incorporates a multidirectional accelerometer to monitor degree and intensity of motion. Actigraphs are approved as medical devices that can measure sleep-wake patterns over a 24 hour period by fitting collected activity data into an algorithm.

The study evaluated four doses of lemborexant (2.5mg, 5mg, 10mg and 15mg) versus placebo. Treatment with lemborexant resulted in an improved 24-hour circadian rhythm pattern with statistically significant reductions in nighttime activity compared to placebo after four weeks of treatment at three of the four doses tested (2.5mg, 5mg, and 15mg). Treatment with lemborexant also helped to consolidate nighttime sleep with positive trends, not statistically significant, for less fragmented and longer total sleep time during the night. Finally, the duration of unintentional daytime naps tended to be shorter with lemborexant treatment compared to placebo.

The most common adverse events were constipation, somnolence, arthralgia, headache and nightmare. Most adverse events were mild to moderate and infrequent. No patients discontinued the study. There was no change with treatment on cognition as measured by the Mini-Mental State Examination (MMSE) or Alzheimer's Disease Assessment Scale for cognition (ADAS-Cog) that would indicate impairment.

"ISWRD is a serious and debilitating condition and coupled with dementia puts patients at risk for falls when awake and wandering in the middle of night and poses considerable burden to the family members and caregivers of these patients," said Phyllis Zee, MD. PhD, Professor of Neurology at Northwestern University. "The results of Study 202 are encouraging for the potential further development of lemborexant

for the treatment of ISWRD."

By acting on the orexin neurotransmitter system, which is the primary regulator of the appropriate balance between sleep and wake at the appropriate circadian times, lemborexant appears to impact the underlying reason for a patient's inability to sleep well.

"Our aspiration is to develop lemborexant as a first-in-class medicine for ISWRD to improve sleep and wake patterns for patients with dementia, and as a best-in-class medicine for insomnia disorder" said Lynn Kramer, MD, Chief Clinical Officer and Chief Medical Officer, Neurology Business Group, Eisai. "We are encouraged by the results of Study 202 in patients with ISWRD and as we conduct additional analyses, we will look forward to engaging experts in the field and health authorities regarding a potential path forward for full development, aiming to contribute to patients through lemborexant."

Eisai is striving to create innovative medicines through a holistic and multi-dimensional approach to dementia drug discovery research based on a foundation of over 30 years of experience of drug discovery activities in the area of Alzheimer's disease / dementia. Through research and development on lemborexant, Eisai is striving to fulfill new unmet medical needs in ISWRD and dementia in addition to insomnia to further contribute to increasing the benefit for patients and their families.

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[Notes to editors]

1. About lemborexant

Lemborexant (development code: E2006), a dual orexin receptor antagonist, is an in-house discovered and developed small molecule compound by Eisai which inhibits orexin by binding competitively to two subtypes of orexin receptors (orexin receptor 1 and 2). In individuals with insomnia disorder, it is possible that the orexin system which regulates sleep and wakefulness is not functioning normally. During normal periods of sleep, orexin system activity is suppressed, suggesting it is possible to purposefully facilitate the initiation and maintenance of sleep by interfering with orexin neurotransmission with lemborexant.

Eisai and Purdue Pharma are investigating lemborexant as a potential treatment option for sleep-wake disorders. In addition to investigation for the potential treatment of ISWRD in patients with Alzheimer's Disease, Eisai and Purdue are developing lemborexant for the treatment of insomnia disorder, and Phase III studies for the treatment of insomnia have now been completed.

Information about ongoing clinical studies is available at clinicaltrials.gov.

2. About ISWRD (Irregular Sleep-Wake Rhythm Disorder)

ISWRD is a type of circadian rhythm sleep disorder where the pattern of sleep and wakefulness that repeats itself over a 24-hour period in healthy individuals is broken down, and sleeping and waking occur instead at various times during the day and night. This is often observed in patients with dementia. Although referred to in this press release as ISWRD, the condition is also known as a Circadian Rhythm Sleep Disorder - Irregular Sleep Wake Type.

3. About Study 202

Study 202 is a multicenter, randomized, double-blind, placebo-controlled, parallel-group Phase II clinical study (with an open-label extension) of the efficacy and safety of lemborexant in subjects with ISWRD and mild to moderate Alzheimer's disease dementia conducted in the United States, Japan and the United Kingdom. Patients with ISWRD associated with Alzheimer's disease were administered 2.5 mg, 5 mg, 10 mg or 15 mg of lemborexant or placebo for 4 weeks to determine whether lemborexant would lead to improvement in circadian rhythm, nighttime sleep or daytime

wake variables, as measured by actigram. Subjects diagnosed with Alzheimer's disease who also met the Diagnostic and Statistical Manual of Mental Disorders - 5th edition (DSM-5) and the 10th revision of the International Classification of Diseases (ICD-10) criteria for ISWRD were screened with actigraphy to ensure current patterns of ISWRD, and then were randomized to one of four doses of lemborexant or placebo. Actigraphy was recorded continuously during the screening period, for the 1-month treatment period, and a 2-week follow-up period.

4. About Actigraphy

An actigraph is a non-invasive device worn on the wrist that incorporates a multidirectional accelerometer to monitor degree and intensity of motion. This device consists of a compact, wrist-worn, battery-operated activity monitor which looks like a wrist watch. Actigraphs are approved as medical devices that can measure sleep-wake patterns over a 24 hour period by fitting collected activity data into an algorithm. As innovative endpoints using actigraphy, Study 202 evaluated the changes in circadian rhythm-related parameters, nighttime sleep-related parameters and daytime wake-related parameters between baseline and the final week of treatment.

5. About Eisai Co., Ltd.

Leveraging the experience gained from the development and marketing of Aricept®, a treatment for Alzheimer's disease and dementia with Lewy bodies, Eisai has been working to establish a social environment that involves patients in each community in cooperation with various stakeholders including the government, healthcare professionals and care workers, and is estimated to have held over ten thousand dementia awareness events worldwide. As a pioneer in the field of dementia treatment, Eisai is striving to not only develop next generation treatments but also to develop diagnosis methods and provide solutions. 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 Neurology and Oncology.

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 https://www.eisai.com.