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Eisai Co., Ltd.

**EISAI DEMONSTRATES EFFICACY OF INVESTIGATIONAL
DUAL OREXIN RECEPTOR ANTAGONIST E2006 IN SLEEP INITIATION AND MAINTENANCE**
*DATA FROM PHASE II CLINICAL TRIAL FOR INSOMNIA PRESENTED AT
53RD AMERICAN COLLEGE OF NEUROPSYCHOPHARMACOLOGY ANNUAL MEETING*

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has presented data from a Phase II clinical study (Study 201) on its in-house-developed investigational dual orexin receptor antagonist (DORA) E2006 in patients with insomnia disorder at the 53rd American College of Neuropsychopharmacology (ACNP) Annual Meeting held from December 7 through 11, 2014, in Phoenix, Arizona in the United States. In the study, E2006 demonstrated a statistically significant improvement in sleep initiation and sleep maintenance without increasing next-day residual sleepiness when compared with placebo.

E2006 is a novel DORA discovered by Eisai. As orexins are neuropeptides that are major regulators of the neural mechanisms underlying sleep and wakefulness, E2006 is being developed for the potential treatment of insomnia disorder. The drug competitively binds to two subtypes of orexin neuron receptors, interfering with orexin neurotransmission to facilitate sleep onset and maintenance.

Study 201 was a multicenter, randomized, placebo-controlled, parallel-group Phase II clinical study conducted in the United States. The primary objective was to identify at least one dose of E2006 that could provide a satisfactory balance of sleep efficiency (total sleep time as a proportion of time in bed) and next-day residual sleepiness. 291 patients with insomnia disorder were randomized to receive 1 of 6 doses of E2006 (1 mg, 2.5 mg, 5 mg, 10 mg, 15 mg, 25 mg) or placebo for 15 days.

Compared to baseline, E2006 statistically significantly improved mean sleep efficiency at all doses. E2006 also shortened both latency to persistent sleep (LPS) and wake after sleep onset (WASO), demonstrating a statistically significant reduction compared to placebo at all dosage amounts of 2.5 mg and higher for LPS, and 10 mg and higher for WASO, respectively. Moreover, the only E2006 group to show a statistically significant increase compared to placebo in next-day residual sleepiness as measured by the Karolinska Sleepiness Scale (KSS) was at the dose of 25 mg.

The most common treatment-emergent adverse events reported in patients treated with E2006 (overall group) were somnolence, headache and sleep paralysis.

Based on the results of study 201, Eisai is making preparations in co-operation with the health authorities in various countries toward conducting Phase III studies for E2006. Eisai considers integrative neuroscience to be a therapeutic area of focus, and is committed to the development of drugs such as E2006. Through these efforts, Eisai is committed to addressing the unmet medical needs that exist in the field of neuroscience and making contributions to further increase the benefits to patients and their families.

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[Notes to editors]

1. About E2006

E2006, a dual orexin receptor antagonist (DORA), is an in-house discovered and developed small molecule compound by Eisai which inhibits orexin by binding competitively to two subtypes of orexin neuron 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 counteract inappropriate wakefulness and facilitate the initiation and maintenance of sleep by interfering with orexin neurotransmission. Therefore Eisai is developing E2006 as a treatment for insomnia.

2. About Study 201

Study Design: Multi-center (within the U.S.), randomized, double-blind, placebo-controlled, parallel-group, Bayesian adaptive, dose response study

Eligibility: Patients between 18 and 80 years old, inclusive, with chronic insomnia as defined by the DSM-5 criteria for insomnia disorder (difficulty sleeping at least 3 times per week for a period of at least 3 months), 291 subjects

Primary Objective: Identify an optimal dose of E2006 that balances sleep efficiency and next-day residual sleepiness

Treatment Method: Patients were given a dose of either E2006 at 1 mg, 2.5 mg, 5 mg, 10 mg, 15 mg, 25 mg or placebo prior to sleep

Treatment Duration: Screening period to determine eligibility and establish baseline sleep parameters, 15 days (nights), followed by 2 days (nights) of placebo to assess rebound insomnia (occurrence of insomnia worse than at baseline after stopping treatment)

Primary Endpoints: Sleep efficiency (SE) as measured by objective polysomnography (PSG) and next-day residual sleepiness as measured by the Karolinska Sleepiness Scale (KSS)

Secondary Endpoints: Latency to persistent sleep (LPS), wake after sleep onset (WASO), Sleep Diary measures of efficacy, objective measures of next-day residual sleepiness, etc.

*Bayesian adaptive design: A multi-stage study that optimally changes (adapts) treatment allocation based on the results of interim analyses

*PSG: A sleep assessment method that records the biophysiological changes that occur during sleep by monitoring designated parameters such as brainwaves, eye movements and skeletal muscle activation

*SE: Total sleep time as a proportion of time in bed

*LPS: Time from lights off to entering persistent sleep

*WASO: Total time spent awake after falling asleep

*KSS: Subjective sleepiness assessment scale developed by the Karolinska Institute