EISAI SUBMITS NEW DRUG APPLICATION FOR MECOBALAMIN ULTRA-HIGH DOSE PREPARATION AS TREATMENT FOR AMYOTROPHIC LATERAL SCLEROSIS IN JAPAN

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, “Eisai”) announced today that it has submitted a new drug application for mecobalamin (development code: E0302) as a treatment for amyotrophic lateral sclerosis (ALS) in Japan.

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Eisai considers neurology a therapeutic area of focus and is committed to new drug development in this field. Furthermore, as a maker and discoverer of new drugs, Eisai is carrying out various initiatives including research into uncovering new indications and value for existing drugs such as mecobalamin in order to fulfill unmet medical needs in neurology and further contribute to increasing the benefit for patients and their families.

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[Notes to editors]

1. About Amyotrophic Lateral Sclerosis (ALS)

ALS is an intractable, progressive, neurodegenerative disease that results in severe muscle atrophy and weakness in the muscles due to motor neuron dysfunction. As the main cause of death is respiratory failure due to paralysis of the respiratory muscles, without the use of an artificial respirator, death occurs within approximately 3 and 6 years from the onset of the disease. In Japan, the incidence rate of ALS ranges between 1.1 to 2.5 per 100,000 people, and onset most often occurs between the ages of 50 to 60. According to the number of patients issued a Certificate of the Recipient of Specified Disease Treatment, there were 9,240 patients with ALS in Japan in 2013. Currently, there is no curative treatment established for ALS, and since there is only one medicine approved for suppressing the progression of ALS in Japan, this is a disease with significant unmet medical needs.

2. About Mecobalamin

Mecobalamin (development code: E0302) is approved and marketed as Methycobal, a 500 μg injection of mecobalamin indicated for the treatment of peripheral neuropathies and megaloblastic anemia caused by vitamin B_{12} deficiency. Methycobal is also approved as a tablet formulation as well as a fine granule formulation indicated for the treatment of peripheral neuropathies. While the mechanism of action of mecobalamin in ALS is not known, it has been suggested in non-clinical research that mecobalamin may have efficacy through a neuroprotective effect and regeneration of nerve axons. Since the 1990s, clinical research has been carried out on ultra-high dose mecobalamin in ALS by a study group on neurodegenerative disease, funded through the Ministry of Health, Labour and Welfare's Specified Disease Treatment Research Program. Short- and long-term trials of intramuscular injection of mecobalamin at 25 mg and 50 mg per day, which is respectively 50 and 100 times the approved dosage of Methycobal, suggested that ultra-high dose mecobalamin could have a clinical effect in ALS, and therefore Eisai has been promoting clinical studies since 2004. Mecobalamin is highly sensitive to light and therefore Eisai has refined its formulation to specifically develop a new freeze-dried injectable preparation that can be administered at a high dose and is easy to use.

3. About the Phase II/III Clinical Study (Study 761) Conducted in Japan

1) Outline of study:

Title of Study	A Phase II/III Study in Patients with Amyotrophic Lateral Sclerosis (ALS)
Study Design	Multicenter, randomized, placebo-controlled, parallel-group, double-blind, comparative study
Treatment Dosage and Administration	Intramuscular injection of mecobalamin 25 mg, 50 mg or placebo twice a week for 182 weeks
Number of Subjects	370 patients (25 mg group: 124 patients, 50 mg group: 123 patients, placebo: 123 patients)

Objectives	Primary Endpoints: Time to event (full-time use of non-invasive ventilation, use of invasive ventilation, or death) Change in the total ALSFRS-R score from the time of completion of the observation period to the final time point

2) Results of study:

Overall Results	Placebo group	25 mg group	50 mg group
Time to event (median)	880 days	1147 days	954 days