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Global, Phase 3b study of Oral Edaravone in ALS

Mitsubishi Tanabe Pharma Corporation (Head Office: Chuo-ku, Osaka; Representative Director: Akihiro Tsujimura; hereinafter, "MTPC"), a member of the Mitsubishi Chemical Group, announced the decision to discontinue the global, multi-center, double-blind, Phase 3b MT-1186-A02 study*1 of oral edaravone in amyotrophic lateral sclerosis (ALS), based on results of a pre-planned futility analysis conducted by an independent data monitoring committee (IDMC) composed of external experts.
The IDMC's recommendation to conclude the study was not based on safety or efficacy concerns, and this decision does not impact the commercial availability of edaravone oral suspension (Japan product name: RADICUT® Oral Suspension 2.1%).

Study MT-1186-A02, which was a postmarketing commitment following the FDA approval of intravenous edaravone, was designed to evaluate the superiority of an investigational once-daily dosing regimen of oral edaravone (105 mg) vs. the approved on/off dosing regimen administered in 28-day cycles, in people with ALS over 48 weeks. A pre-planned futility analysis, conducted after 50% of the planned study population reached 48 weeks, assessed the study's primary endpoint and the probability of the study results changing if all participants completed the 48-week study period. Through that interim analysis, the IDMC concluded that there is a low statistical probability for the investigational once-daily dosing regimen to show superiority to the current on/off dosing regimen as measured by the ALS Functional Rating Scale Revised (ALSFRS-R) score at study completion; therefore, study discontinuation was recommended by the IDMC.
Preliminary findings of the futility analysis suggest that the efficacy of the approved on/off dosing regimen of oral edaravone was consistent with results of the pivotal Phase 3 trial (MCI186-19 or Study 19) that supported the approval. MT-1186-A02 found no new safety concerns.
As part of this decision, the global, multi-center, double-blind, Phase 3b MT-1186-A04 study*2, an extension to MT-1186-A02, will also be discontinued.

MTPC will apply our learnings from this study to further progress ALS treatment, including real-world evidence and biomarker data research.

*1 Efficacy and Safety Study of Oral Edaravone Administered in Subjects With ALS - Full Text View - ClinicalTrials.gov
*2 Efficacy and Safety Extension Study of Oral Edaravone Administered in Subjects With ALS - Full Text View - ClinicalTrials.gov

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■Amyotrophic Lateral Sclerosis: ALS

ALS is an idiopathic neurodegenerative disease in which motor neurons selectively degenerate and vanish. Muscle strength declines throughout the entire body, including the extremity, facial, and respiratory muscles, and muscular atrophy progresses. While the cause for the majority of cases is not well understood but may involve genetic and environmental factors. It is one of the most well-known neuromuscular diseases and incidence is approximately two in 100,000 people per year worldwide.

■ RADICUT® Oral Suspension 2.1%

RADICUT® Oral Suspension 2.1% is specifically formulated for patients with ALS and provides a flexible administration option with 5 mL dose (taken orally or via feeding tube), a portable bottle, an oral dosing syringe and no need for refrigeration or reconstitution. One cycle of administration of RADICUT® Oral Suspension 2.1% is a total of 28 days, including both the dosing period and the drug-free period, and that cycle is repeated. The first cycle has a dosing period of 14 consecutive days of administration followed by a drug-free period of 14 days. In subsequent cycles, patients receive daily dosing for 10 days within a 14-day dosing period, followed by a 14-day drug-free period. RADICUT® Oral Suspension 2.1% needs to be refrigerated during the distribution process and in pharmacies, but patients can keep it at room temperature.

■Edaravone

Edaravone is a free radical scavenger discovered by MTPC. It was approved by the Ministry of Health, Labour and Welfare in April 2001 for the treatment of patients with acute ischemic stroke and is marketed in Japan under the product name of Radicut®. The indication of ALS has been approved in 11 countries including Japan in June 2015, South Korea in December 2015, the U.S. in May 2017, Canada in October 2018, and Switzerland in January 2019.

Edaravone (oral suspension) for the treatment of ALS was approved in the U.S. in May 2022, in Canada in November 2022 and in Japan in December 2022 (Japan product name: RADICUT® Oral Suspension 2.1%).

■MT-1186-A02 study

Study MT-1186-A02, which was a postmarketing commitment following the FDA approval of intravenous edaravone (RADICAVA®), was designed to evaluate the superiority of an once-daily dosing regimen of oral edaravone (105 mg) vs. the approved on/off dosing regimen administered in 28-day cycles, in people with ALS over 48 weeks. The planned subject number is approximately 380. The primary endpoint is the change in ALSFRS-R score from baseline to 48 weeks.

Based on the results of the pre-planned futility analysis, the FDA released Mitsubishi Tanabe Pharma America, Inc., a wholly-owned subsidiary of Mitsubishi Tanabe Pharma Corporation, of its postmarketing commitment.