

POST-HOC ANALYSES OF RADICAVA[®] (EDARAVONE) STUDIES SHOW PHASE 3 STUDY DESIGN MINIMIZED ALS HETEROGENEITY TO IMPROVE TRIAL EFFICIENCY

Strategic Inclusion Criteria Enabled Detection of Efficacy Intended to be Generalizable to Larger ALS Population

JERSEY CITY, N.J., May 2, 2019 – Mitsubishi Tanabe Pharma America, Inc. (MTPA) today announced results from a post-hoc analysis that showed how the RADICAVA[®] (edaravone) Phase 3 study design minimized heterogeneity of the study population to successfully demonstrate a treatment effect in amyotrophic lateral sclerosis (ALS) in 24 weeks.¹ Because ALS is a heterogeneous disease, and no two patients follow the exact same trajectory of decline over time, demonstrating a clinical response in trials can be challenging.² The findings, published in *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, illustrate the importance of employing enrichment strategies when designing studies in ALS.

“Prior to the successful pivotal Phase 3 trial of RADICAVA, for many years the ALS research community had struggled to identify a new medicine able to show an effect on disease progression,” said Joseph M. Palumbo, M.D., Vice President, Mitsubishi Tanabe Pharma Development America, Inc. “Our researchers focused on slowing progressive functional change in the core signs and symptoms of ALS, minimizing the effect of disease heterogeneity, and showing that the efficacy of RADICAVA could be generalized to a larger population.”

When analyzing results from a prior Phase 3 trial (Study 16), researchers determined that the level of variability and rate of progression seen among study participants may have made it difficult to detect a prospective treatment effect. The patient population for the pivotal Phase 3 study (Study 19) was enriched with participants who would have tendency for disease progression, as measured by the ALS Functional Rating Scale-Revised (ALSF_{RS}-R), during the 24-week study time frame. Study authors concluded that reducing the number of slow progressing patients in Study 19 showed a treatment effect with edaravone at 24 weeks.³

RADICAVA is approved as a treatment option for ALS by regulatory authorities in the U.S., Japan, South Korea, Canada and Switzerland based on the results of Study 19. Key learnings from this successful development program may contribute to further refinement of ALS trials and rare disease trials.

In addition, MTPA will present pharmacokinetic data and development plan details on the investigational [oral suspension formulation](#) of edaravone in a poster session at the 2019 American Academy of Neurology (AAN) Annual Meeting, being held May 4-10 in Philadelphia. The poster session will be held on Sunday, May 5, from 11:30 a.m. – 6:30 p.m. ET (Poster Session P1: Amyotrophic Lateral Sclerosis).

About Mitsubishi Tanabe Pharma America, Inc.

Based in Jersey City, N.J., Mitsubishi Tanabe Pharma America, Inc. (MTPA) is a wholly-owned subsidiary of Mitsubishi Tanabe Pharma Corporation's (MTPC) 100 percent owned U.S. holding company, Mitsubishi Tanabe Pharma Holdings America, Inc. MTPA is dedicated to delivering innovative products that address the unmet medical needs of patients in North America. It was established by MTPC to commercialize approved pharmaceutical products in North America with plans to expand its product line through collaborations with partners. For more information, please visit www.mt-pharma-america.com or follow us on [Twitter](#) and [Facebook](#).

Overview of Mitsubishi Tanabe Pharma Corporation

Mitsubishi Tanabe Pharma, which was founded in 1678, has its headquarters in Doshomachi, Osaka, which is the birthplace of Japan's pharmaceutical industry. With business centered on ethical pharmaceuticals, Mitsubishi Tanabe Pharma is a well-established company and has the longest history of any listed company in Japan.⁴ In accordance with the corporate philosophy of "contributing to the healthier lives of people around the world through the creation of pharmaceuticals," the Company formulated the key concept of Open Up the Future under the Medium-Term Management Plan 2016-2020. Through the discovery of drugs that address unmet medical needs, centered on its priority disease areas — autoimmune diseases, diabetes and kidney diseases, central nervous system diseases, and vaccines — Mitsubishi Tanabe Pharma will strive to contribute to the health of patients around the world. MTPC is the parent company of MTPA and the license holder of RADICAVA. For more information, go to <http://www.mt-pharma.co.jp/>.

About RADICAVA[®] (edaravone) IV

The U.S. Food and Drug Administration (FDA) approved RADICAVA[®] (edaravone) on May 5, 2017 as a treatment for amyotrophic lateral sclerosis (ALS).⁵ In a pivotal clinical trial, people given RADICAVA experienced on average a 33 percent slower loss of physical function, compared to placebo as measured by the ALS Functional Rating Scale-Revised (ALSFRS-R), a validated rating instrument for monitoring the progression of disability in people with ALS.^{2,3,5}

Edaravone was discovered and developed for ALS by Mitsubishi Tanabe Pharma Corporation (MTPC) and commercialized in the U.S. by Mitsubishi Tanabe Pharma America, Inc. MTPC group companies began researching ALS in 2001 through an iterative clinical platform over a 13-year period. In 2015, edaravone was approved for use as a treatment for ALS in Japan and South Korea. Marketing authorization was granted in Canada in October 2018 and Switzerland in January 2019.

IMPORTANT SAFETY INFORMATION

Before you receive RADICAVA, tell your healthcare provider about all of your medical conditions, including if you:

- have asthma.
- are allergic to other medicines.
- are pregnant or plan to become pregnant. It is not known if RADICAVA will harm your

unborn baby.

- are breastfeeding or plan to breastfeed. It is not known if RADICAVA passes into your breast milk. You and your healthcare provider should decide if you will receive RADICAVA or breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of RADICAVA?

- RADICAVA may cause serious side effects including hypersensitivity (allergic) reactions and sulfite allergic reactions.
- Hypersensitivity reactions have happened in people receiving RADICAVA and can happen after your infusion is finished.
- RADICAVA contains sodium bisulfite, a sulfite that may cause a type of allergic reaction that can be serious and life-threatening. Sodium bisulfite can also cause less severe asthma episodes in certain people. Sulfite sensitivity can happen more often in people who have asthma than in people who do not have asthma.
- Tell your healthcare provider right away or go to the nearest emergency room if you have any of the following symptoms: hives; swelling of the lips, tongue, or face; fainting; breathing problems; wheezing; trouble swallowing; dizziness; itching; or an asthma attack (in people with asthma).
- Your healthcare provider will monitor you during treatment to watch for signs and symptoms of all the serious side effects.

The most common side effects of RADICAVA include bruising (contusion), problems walking (gait disturbance), and headache.

These are not all the possible side effects of RADICAVA. Call your healthcare provider for medical advice about side effects. You may report side effects to Mitsubishi Tanabe Pharma America, Inc. at 1-888-292-0058 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For more information, including full Prescribing Information and Patient Information, please visit www.RADICAVA.com.

Media inquiries:

Debbie Etchison

908-340-8578

Media_MTPA@mt-pharma-us.com

¹ Palumbo J, Hubble J, Apple S, et al. (2019). Post-hoc analyses of the edaravone clinical trials Study 16 and Study 19: a step toward more efficient clinical trial designs in amyotrophic lateral sclerosis. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*. <https://doi.org/10.1080/21678421.2019.1599955>.

² Simon N, Turner, M, Vucic S, et al.(2014). Quantifying Disease Progression in Amyotrophic Lateral Sclerosis. *Annals of Neurology*, 76(5), 643–657. <http://dx.doi.org/10.1002/ana.24273>.

³ The Writing Group on behalf of the Edaravone (MCI-186) ALS 19 Study Group (2017). Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial. *Lancet Neurology*. 16(7), 505-512. [http://dx.doi.org/10.1016/S1474-4422\(17\)30115-1](http://dx.doi.org/10.1016/S1474-4422(17)30115-1).

⁴ Research by TOKYO SHOKO RESEARCH, LTD.

⁵ RADICAVA® U.S. Prescribing Information. August 2018.