Mitsubishi Tanabe Pharma America

Press Release

MITSUBISHI TANABE PHARMA AMERICA ANNOUNCES COLLABORATION WITH MASSACHUSETTS GENERAL HOSPITAL ON ALS BIOMARKER STUDY

Findings May Help Advance Understanding of ALS Diagnosis and Treatment

JERSEY CITY, N.J., March 28, 2019 – Mitsubishi Tanabe Pharma America, Inc. (MTPA) today announced a collaboration with the Massachusetts General Hospital (MGH) Neurological Clinical Research Institute (NCRI) to conduct a study designed to identify and measure specific biomarkers in people with amyotrophic lateral sclerosis (ALS).

"We are honored to be working with the team at MGH on our first clinical trial in the U.S.," said Stephen Apple, M.D., Senior Medical Director, Medical Affairs, MTPA. "This biomarker trial has sparked exponential interest in the ALS community, and with the help of MGH, we hope to further our understanding of the potential role these measures may have in evaluating a treatment response."

The ALS biomarker study, which will be sponsored by MTPA and led by MGH, has been designed to have 200 patients complete six cycles (24 weeks) of treatment, and will be conducted at up to 40 sites across the country. Findings may assist with identifying specific biomarkers as quantifiable, biological, non-clinical measures for the treatment effect of edaravone in people with ALS. The first biomarker study patient is anticipated to be enrolled late spring of 2019, with early interim analyses planned for later in the year.

"ALS is a complex disorder with diverse pathophysiology, and we do not currently have validated biomarkers for diagnosing or following ALS progression," said study Primary Investigator James Berry, M.D., M.P.H., MGH NCRI, Boston. "This study will broaden our understanding of numerous biomarkers that may be associated with ALS, including those for oxidative stress, inflammation, muscle and neuronal injury and death. It will increase our understanding of ALS and of the biological effects of edaravone in people with ALS undergoing therapy."

The biomarker study is a 24-week, prospective, observational, longitudinal, multicenter study. All participants will be newly prescribed commercial RADICAVA® (edaravone) and, once enrolled in this study, biomarker and clinical assessments will be obtained prior to initiating RADICAVA, as well as at start of treatment and at pre-specified time points throughout the study. Patient biomarker data and disease progression assessments will be compared to samples stored at biorepositories and progression models, respectively.

The study will evaluate the following biomarkers:

- **Oxidative stress** – 4-hydroxynonenal (4-HNE), 8-Isoprostanes, 3-nitrotyrosine (3NT), 8-hydroxy-2'-deoxyguanosine (8OHdG), urate
- **Inflammation** – matrix metalloproteinase-9 (MMP-9)
- **Neuronal injury and death** – neurofilament (Nf) heavy and light chain proteins, urinary neurotrophin receptor p75
- **Muscle injury** – creatinine

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 (MTPC)

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.[1] 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)

The U.S. Food and Drug Administration (FDA) approved RADICAVA® (edaravone) on May 5, 2017 as a treatment for amyotrophic lateral sclerosis (ALS).[2] In a pivotal trial, people given RADICAVA experienced a 33 percent slower rate of decline in the 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.[1,3,4]

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 February 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:
Mitsubishi Tanabe Pharma America
Debbie Etchison
908-340-8578
Media_MTPA@mt-pharma-us.com

---

[1] Research by TOKYO SHOKO RESEARCH, LTD.

[2] RADICAVA® U.S. Prescribing Information. August 2018.

[3] Simon, N. G., Turner, M. R., Vucic, S., Al-Chalabi, A., Shefner, J., Lomen-Hoerth, C., & Kiernan, M. C. (2014). Quantifying Disease Progression in Amyotrophic Lateral Sclerosis. *Annals of Neurology*, 76(5), 643–657. http://dx.doi.org/10.1002/ana.24273.

[4] 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.