Mitsubishi Tanabe Pharma America

Press Release

MITSUBISHI TANABE PHARMA AMERICA ANNOUNCES COLLABORATIVE STUDY TO IDENTIFY AND MEASURE BIOMARKERS IN PEOPLE WITH ALS

Findings Will Help Further Understanding of ALS Disease Progression and Treatment Effect

JERSEY CITY, N.J., Dec. 6, 2018 – Mitsubishi Tanabe Pharma America, Inc. (MTPA) today announced it will conduct a study to identify and measure specific biomarkers in people with amyotrophic lateral sclerosis (ALS). The findings may assist researchers and clinicians in starting the process of validation and the use of biomarkers as quantifiable, biological, non-clinical measures for disease progression and treatment effect of edaravone in people with ALS. Interim data are expected in 2019.

"Biomarker research and discovery may be important in the care for people with ALS," said Atsushi Fujimoto, President, MTPA. "Our goal is to evaluate biomarkers in order to gain insights into how the disease progresses, and to potentially optimize research and treatment."

The 24-week, prospective, observational, longitudinal, multicenter study will evaluate approximately 200 adults with ALS in 30 sites across the U.S. 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 bio-banked natural history of disease samples and disease progression models.

"We are honored that MTPA has chosen Origent Data Sciences, with its progression models, to participate in this study," said Dave Ennist, Chief Science Officer, Origent Data Sciences. "We are eager to see insights from the prospective application of our models, which will be utilized as virtual controls to analyze treatment outcomes and provide insights to support the ALS community."

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 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 clinical trials, 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.[2,3,4]

RADICAVA is administered in 28-day cycles by intravenous infusion. It takes 60 minutes to receive each 60 mg dose. For the initial cycle, the treatment is infused daily for 14 consecutive days, followed by a two-week drug-free period. All cycles thereafter are infused daily for 10 days within a 14-day period, followed by a two-week drug-free period.[2]

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, and in 2018, the treatment was approved in Canada.

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**.

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.[5] 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/.

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About Origent Data Sciences, Inc.

Origent Data Sciences, Inc. is a spinoff of Sentrana, Inc., a pioneer in the field of Precision Sales and Marketing and winner of the DREAM Phil Bowen ALS Prediction Prize4Life Challenge. Since that time, Origent has become the market leader in clinical trial optimization leveraging patient-level predictive modeling for neurological conditions including ALS, and has developed many new applications to manage and reduce drug development risks through better foresight. Rather than considering a similar historic patient to act "the same" as a current patient, Origent treats and models each patient separately, predicting their behavior individually. By modeling patient-level dynamics rather than the characteristics of a population, Origent's tools uncover a deep level of insight that allows biostatisticians and researchers to gain clearer understanding and greater knowledge from their data. For additional information about Origent, visit http://www.origent.com/.

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[1] Benatar M, Boylan K, Jeromin A, et al. ALS biomarkers for therapy development: state of the field and future directions. *Muscle Nerve*. 2016;53(2):169-182.

[2] RADICAVA® U.S. Prescribing Information. August 2017.

[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.

[5] Research by TOKYO SHOKO RESEARCH, LTD.