



The ALS Association
National Office

Media Release

27001 Agoura Road, Suite 150
Calabasas Hills, CA 91301-5104
(818) 880-9007 FAX (818) 880-9006

Contact:
The ALS Association
Gary Wosk
(818) 587-2241
gwosk@alsa-national.org

The ALS Association to Support Trial of Lithium

CALABASAS HILLS, Calif. (August 28, 2008) -- The ALS Association is funding a major clinical trial to determine if lithium can slow disease progression in patients in the early stages of ALS (amyotrophic lateral sclerosis), commonly referred to as Lou Gehrig's Disease. The study builds on earlier promising results from preclinical research and a small, open-label investigation in ALS patients.

"Lithium has generated a lot of interest in the ALS community," according to Lucie Bruijn, Ph.D., senior vice president, research and development of The Association. "This trial is vital for testing the efficacy of lithium in a well-controlled way. It's the crucial next step for investigating the potential of this drug."

The trial is being supported through The Association's TREAT ALS (T**ranslational R**esearch Advancing Therapies for ALS) initiative, and will use the TREAT ALS/NEALS Clinical Trials Network. Lead investigators for the study will be Merit Cudkowicz, M.D., and Swati Aggarwal, M.D., of Massachusetts General Hospital, Lorne Zinman, M.D., from the University of Toronto, Petra Kaufman, M.D., from Columbia University, and Jeremy Shefner, M.D., of SUNY Upstate Medical University.

In addition to The Association, funding partners for the new study include the National Institutes of Health/ National Institute of Neurological Disorders and Stroke and ALS Society of Canada. Investigators worked together with the funding agencies to design the most appropriate study within the shortest possible time frame. "Collaboration among researchers and funding agencies makes this trial possible," Dr. Bruijn said. "All of us are working together to support this important research to find a new treatment for ALS."

Lithium is a simple chemical substance approved for use in humans and prescribed as a mood stabilizer. Lithium protects neurons in the brain in animal models of neurodegenerative diseases, including Alzheimer's disease and Parkinson's disease, and has been recently shown to do the same in a mouse model of ALS. In that study, lithium prolonged survival and protected cells in

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both the brain and spinal cord. While the exact mechanism of lithium's effect is unknown, researchers have proposed it promotes clearance of toxic protein accumulation.

A study in a small number of ALS patients compared lithium plus riluzole (an approved treatment for ALS) to riluzole alone. After 15 months, no deaths occurred in the 16 participants treated with lithium plus riluzole, while 29% of those taking riluzole alone had died. Patients on lithium also had a markedly lower decline in disease-related disability. However, the trial was limited by the small numbers of patients and the absence of a placebo treatment — both the patient and the doctor knew whether the patient was taking lithium or not, which may have influenced the response to treatment or interpretation of disability. Due to diagnostic and prognostic variability in persons showing symptoms of ALS, the small numbers in this study were not sufficient to know whether lithium was indeed an effective treatment. Many apparently effective treatments in open trials (trials lacking a concurrent placebo group) fail in larger double-blind trials, in which neither doctor nor patient knows whether the patient is receiving the study drug.

The new trial will be a double-blind, placebo-controlled trial with 84 patients, who will be randomized to either lithium or placebo. A review of data will occur after the 84th person is enrolled, and then a decision will be made on whether to expand to 250 patients. Patients may be included if they are within three years of their diagnosis and are not already taking lithium. Treatment will be for up to one year. The disease course and safety assessments will be measured at regular intervals over that time. Further details including trial sites, enrollment criteria and start dates will follow shortly. "We formed collaboration with Canadian and U.S. sites to perform a study that will provide an answer quickly on whether lithium is effective in the treatment of ALS. The study is designed to answer this key question definitively and with appropriate monitoring of safety," commented Merit Cudkowicz, M.D., one of the lead investigators on the study.

Denise Figlewicz, Ph.D., director of research at the ALS Society of Canada said, "We welcome this opportunity to support the lithium clinical trial. The promising results from the Italian study data serve as the impetus for new research and new treatment strategies. This is very exciting news for the ALS community. We also welcome this opportunity to work together with our American colleagues. This collaborative approach between Canada and the United States will serve as a model for subsequent clinical trials."

ALS and The ALS Association

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord. Motor neurons reach from the brain to the spinal cord and from the spinal cord to the muscles throughout the body. When the motor neurons die, the ability of the brain to initiate and control muscle movement is lost, leading to progressive paralysis.

The ALS Association is the only national, not-for-profit voluntary health organization devoted solely to fighting ALS through research, patient services, advocacy and public education and information. TREAT ALS is a drug discovery program and clinical trials process created by The Association that accelerates discovery and testing of clinical candidates.

