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FOR IMMEDIATE RELEASE**SCIENTISTS DISCOVER WHY ANIMAL STUDIES MAY LEAD TO INEFFECTIVE ALS DRUGS
*Study Recommends Guidelines for Using Leading Mouse Model of ALS***

CAMBRIDGE, Mass., January 22, 2008 — A five-year study of more than 70 drugs, many with reported survival benefit in a mouse model of the inherited form of amyotrophic lateral sclerosis — ALS or Lou Gehrig's Disease, concluded the apparent positive effects were largely due to previously unrecognized variables in the study design, scientists reported today. The study included the drug riluzole, the only drug approved by the U.S. Food and Drug Administration for ALS treatment.

The study was undertaken to evaluate possible ALS treatments, and to put money and resources behind the most promising ones. Despite the findings, the investigators said the study establishes guidelines for evaluating preclinical mouse studies in ALS, and provides a starting point for standardizing the use of this animal model of ALS.

“Researchers have been puzzled as to why animal results have failed to replicate in the clinic,” said Sean A. Scott, the principal investigator and president of the Cambridge-based ALS Therapy Development Institute, which conducted the study. “It appears this animal model is subject to greater variability than many investigators realized. The exciting part of this study is that one can now identify and substantially eliminate the biological variability to fully exploit the value of this animal model for identifying effective treatments.”

Scientists screened the drugs in 18,000 genetically engineered mice, across 221 independent studies, only to find no significantly positive outcomes for any of the compounds previously thought to extend the lifespan of the ALS mouse commonly used in preclinical studies. The study was published in Internet edition of the journal, *Amyotrophic Lateral Sclerosis*.

“We expected to replicate previous reports of efficacy and to establish both positive controls and metrics to gauge future therapeutic potential,” added Scott. “While we were able to measure a significant difference in survival between males and females, we observed no significant positive or negative effects for any of the 70-plus compounds tested, including several previously reported as efficacious.”

According to Sharon Hesterlee, Ph.D., vice president, translational research for the Muscular Dystrophy Association, the Institute's capacity to conduct industrial-scale research laid the groundwork for the MDA's decision to form a three-year, \$36 million research collaboration with it last year. “This important study highlights the need to better understand and to standardize the field's use of this mouse model of ALS, particularly when it's used as the basis for launching a human clinical trial.”

Through sophisticated computer modeling and data mining, the researchers were able to determine that the discrepancies in previous studies were largely caused by biological and genetic differences, including animal gender. Unless the studies were tightly controlled, noise in the experimental system would swamp most signals and could be interpreted as a positive result.

The research failed to replicate several studies in the SOD1 mouse model that have led to clinical

trials of drugs that showed promise for treating ALS. Their results showed the compounds minocycline, creatine, ritonavir, celecoxib, sodium phenylbutyrate, ceftriaxone, WHI-P131, thalidomide, and riluzole had no survival benefit at their reported routes and doses. The therapeutic effect of the FDA-approved drug riluzole is known to be marginal, providing on average only two months extended survival in ALS patients.

“When we put these results in the context of the millions of dollars spent on ALS research, one can appreciate the huge economic impact a study of this kind can have,” said Augie Nieto, chairman of the ALS Therapy Development Institute. “This study shows how rigorous research can be accomplished through the power of a nonprofit mission that brings together patients, doctors and researchers toward finding a cure for ALS and other neuromuscular diseases.” Nieto and his wife serve as co-chairpersons of MDA's ALS Division. Nieto received a diagnosis of ALS in March 2005.

About ALS

ALS is a chronic, progressive neurodegenerative disease that leads to paralysis due to the death of motor neurons in the spinal cord and brain. Patients become trapped within their bodies, unable to speak, eat, or breathe on their own. Most succumb to respiratory failure within three to five years of diagnosis. A small percentage of ALS in humans is caused by a mutation in the gene coding for the SOD1 protein, an enzyme that helps prevent oxygen toxicity in cells. It's not known what ultimately causes sporadic ALS, which constitutes some 95% of all disease cases.

ALS strikes 2:100,000 Americans per year, typically in middle or old age, with a slight preference for males. There are approximately 30,000 diagnosed patients in the United States, with a similar number in Europe. Approximately 90% of cases are sporadic and 5% to 10% are familial. About 20% of ALS patients live 5 years or more, 10% survive more than 10 years, and 5% live 20 years after diagnosis. Quality of life becomes a huge challenge for patients. In later stages of the disease, patients are alert mentally but functionally quadriplegic in many cases, aware of impending death. The cost of care at later stages reaches an average of \$200,000 per year.

About ALS Therapy Development Institute

The ALS Therapy Development Institute (www.als.net), based in Cambridge, Mass., operates the world's largest research and development program focused exclusively on ALS. Its staff of 30 scientists and research technicians work on behalf of ALS patients to discover and advance novel therapeutics for treating and ultimately curing ALS. The non-profit biotechnology institute excels in identifying novel disease targets, discovering compounds that may act against these targets, and screening potential treatments for clinical development.

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