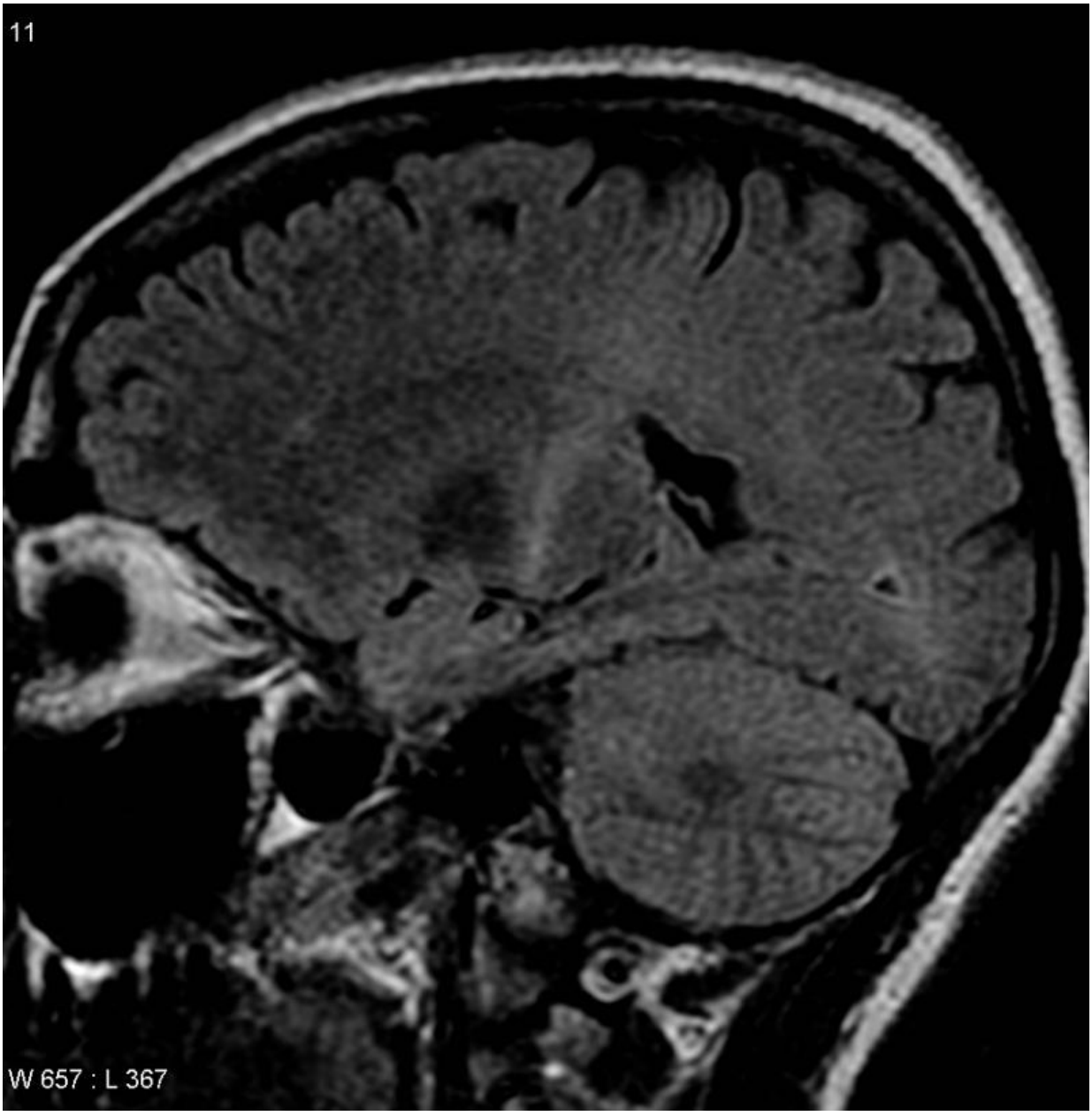
Investigational ALS drug generates promising clinical trial results

September 2 2020



An MRI with increased signal in the posterior part of the internal capsule which can be tracked to the motor cortex consistent with the diagnosis of ALS. Credit: Frank Gaillard/Wikipedia

An experimental medication slows the progression of the neurodegenerative disease called Amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, according to recently released results from a clinical trial run by investigators at the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital (MGH) and Amylyx Pharmaceuticals, Inc., the company that manufactures the medication. The findings, reported in the *New England Journal of Medicine*, offer hope that a treatment may one day be available for patients with ALS, a fatal condition with no cure that attacks the nerve cells in the brain and the spinal cord to progressively hinder individuals' ability to move, speak, eat, and even breathe.

Called AMX0035, the oral medication is a combination of two drugs, sodium phenylbutyrate and taurursodiol, that each target a different cell component important for protecting against nerve cell death.

In the CENTAUR trial, 137 participants with ALS were randomized in a two-toone ratio to receive AMX0035 or placebo. Over six months, participants who were treated with AMX0035 had better functional outcomes than those treated with placebo as measured by the ALS Functional Rating Scale (ALSFRS-R), a questionnaire that evaluates several activities of daily living such as a patient's ability to walk, hold a pen or swallow food.

"The participants treated with AMX0035 demonstrated a significant slowing of ALS disease progression as measured by the ALSFRS-R.

This is a milestone in our fight against ALS," said Sabrina Paganoni, MD, Ph.D., principal investigator of the CENTAUR study, investigator at the Healey & AMG Center for ALS at MGH, and assistant professor of PM&R at Harvard Medical School (HMS) and Spaulding Rehabilitation Hospital. Paganoni noted that the trial involved a partnership between industry, foundations such as the ALS Association and ALS Finding a Cure and academia, with input from world-renowned leaders in neurology and drug development.

Senior author Merit Cudkowicz, MD, director of the Healey & AMG Center for ALS at MGH, chief of Neurology at MGH, and the Julieanne Dorn Professor of Neurology at HMS, commented, "Amylyx took a novel approach to the problem of motor nerve cell dysfunction. With guidance from our team and in collaboration with our colleagues in the Northeast ALS Consortium (NEALS), Mass General Biostats and the Barrows Neurological Institute, the clinical trial moved forward quickly and carefully. We are proud of this important study. We are also very thankful to the participants and their families for their key role in advancing research."

In 2015, Amylyx co-founders and co-CEOs Joshua Cohen and Justin Klee were introduced to Cudkowicz through a colleague and shared their vision for AMX0035. The teams decided that MGH's expertise in designing and leading clinical trials and Amylyx's potential treatment would make for a great collaboration. Cudkowicz introduced them to Paganoni and to the science advisory committee for NEALS, a trial network Cudkowicz co-founded. Soon after, the CENTAUR Trial came to fruition and sites throughout the NEALS consortium began enrolling patients.

"Today's news builds upon the progress we have made in ALS research," said Cohen. "This experimental medicine has demonstrated that it can help patients retain their physical function, which is an incredible feat

given the debilitating nature of this disease. It is our hope that AMX0035 will one day be available for patients and we are committed to making that a reality."

"Patients and their families do not have time to wait," said Klee. "People with ALS progressively lose their ability to function and care for themselves, so we want to do everything we can to help them slow down this devastating disease. We will be working with the FDA to determine next steps and the path for patients to gain access to AMX0035. We'll continue to share our plans with the community as they develop."

An Open Label Extension trial, in which all patients in the study have been offered AMX0035, is ongoing to assess the medication's long-term impact.

More information: *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa1916945

Provided by Massachusetts General Hospital