Until recently, there has been no lab test to confirm a diagnosis of ALS, or to track its progression. But such tests would be very valuable for achieving the earliest possible diagnosis of the disease, allowing immediate treatment once it becomes available. And clinical researchers agree that the ability to precisely track progression is critical for testing whether a new therapy can slow or halt progression of the disease.

Development of lab tests for diagnosing and tracking ALS is the mission of Iron Horse Diagnostics. The company name comes from Lou Gehrig, who was known as the Iron Horse and died of ALS. Recently, the two leaders of the company, Robert Bowser, Ph.D., and Andreas Jeromin, Ph.D., spoke in a webinar to present an update of the exciting progress the company has made, with the help of The ALS Association, in reaching their goals. Dr. Bowser, who is Director of the ALS and Neuromuscular Center at Barrow Neurologic in Phoenix, Arizona, is President of Iron Horse, and Dr. Jeromin is Chief Scientific Officer.

“Diagnosis takes time and is costly,” Dr. Jeromin said. It can typically take up to a year to receive a confirmed diagnosis of ALS and cost more than $10,000. A principal problem is that there are many other conditions that mimic the disease in its early stages.

Iron Horse has developed a set of lab tests that measure the levels of key proteins in the blood or cerebrospinal fluid (CSF). The levels of these proteins are higher in people with ALS than in those with other neurologic diseases or in healthy subjects. The tests are fast, with results returned to the physician within a week of taking the samples. “We envision this will dramatically change the way ALS is diagnosed and treated,” Dr. Jeromin said.

The proteins measured are markers of two key aspects of the ALS disease process. One protein, called “phosphorylated neurofilament heavy chain,” is increased when neurons are damaged. The second, called “complement C,” indicates ongoing inflammation, which contributes to neuronal damage as well. The proteins are detected using antibodies in a type of test called “enzyme-linked immunosorbent assay” (ELISA).

Dr. Bowser explained that the Iron Horse tests have been validated through testing at 23 medical centers across the country. A blood test alone is 75% accurate for diagnosis of ALS and may serve as a useful screening test. A combination of the blood test and the CSF test is 93% accurate, in line with diagnostic tests for many other diseases. It is the physician who makes the
final diagnosis, Dr. Bowser stressed, and the tests are meant to help the physician come to the correct diagnosis quickly.

The combination diagnostic test is currently undergoing a final validation study in 300 patients, after which Iron Horse will seek FDA approval for the test to be used at laboratories throughout the country. It is currently available at two labs, one at Iron Horse and another at an affiliated laboratory. The team is currently working with insurance companies to obtain a billing code, making the test eligible for insurance reimbursement.

Emerging evidence indicates the test may also be useful for tracking disease progression over time. Drs. Bowser and Jeromin have found that the level of phosphorylated neurofilament heavy chain increases over the course of the disease, and the rate of increase correlates with severity of progression. “We think we can use this to help determine if a drug is having a positive effect in patients,” Dr. Bowser said.

The goal would be to measure the protein at the start of treatment to see if treatment slowed the predicted increase in protein in line with change in clinical measures, such as the ALS Functional Rating Scale. This would allow the test to be used as a biomarker for progression that would more rapidly detect whether a drug was having a beneficial effect. This is an important goal for speeding clinical trials in ALS.

“This is extremely exciting,” said ALS Association Chief Scientist Lucie Bruijn, Ph.D., M.B.A, who hosted the webinar. “It is incredible to see a clear diagnostic test developed for ALS. We are very anxious to see how this work progresses.”