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Avicena Drug Misses Endpoint But Shows Improved Mortality

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Washington Editor

Phase III data pointed to improved mortality outcomes among amyotrophic lateral sclerosis (ALS) patients treated with an investigational drug called ALS-02, though the study failed to meet its primary and secondary endpoints.

Nevertheless, the positive trend was cause for hope for Avicena Group Inc., the company behind the compound.

The mortality findings were pulled from an analysis of the Phase III study and additional mortality data from a previous Phase II study, demonstrating a trend toward decreased mortality in those who received ALS-02. In fact, there was a significant improvement in that outcome for ALS-02 patients compared to those who received placebo, though the company has yet to disclose the numbers.

"We feel that there's a lot of promise," said Avicena CEO Belinda Tsao-Nivaggioli. "The fact that we can reduce mortality, or death, by quite a bit means a lot to these patients."

She told *BioWorld Today* that while the findings were "unexpected," the Palo Alto, Calif.-based company would work to advance the profile of the compound, which is a clinical form of creatine. It has orphan drug status from the FDA.

Investors took note of the data and gave Avicena's shares (OTCBB:AVGO) a slight nudge Tuesday, with the stock gaining 26 cents to close at \$4.70.

The company went public in March by directly selling 21 million shares to private investors through an Over-the-Counter Bulletin Board listing, a quicker route to public markets than a traditional IPO would have been, Tsao-Nivaggioli said.

The multicenter, double-blinded, randomized study showed no statistically significant difference between ALS-02 and placebo with regard to primary and secondary endpoints that included various measures of muscle

strength, muscle fatigue and functional scores. But the drug, which was administered daily in a 5-gram dose for nine months, was found to be safe and well tolerated.

ALS-02's neuroprotective qualities arise from its foundation in creatine, which Tsao-Nivaggioli said acts "as a booster for ATP production." The creatine provides energy to neurons that are dying from ALS, allowing them to live longer. Essentially, the creatine kinase system is being harnessed to enhance energy production.

The trial was supported by the National Center for Complementary and Alternative Medicine, a component of the National Institutes of Health in Bethesda, Md.

In a continuing analysis, data on all Phase III outcome measures are being combined with those from the previously completed Phase II trial, which was conducted by the North East ALS Consortium. Also, a meta-analysis is being planned to merge data from the two trials of ALS-02 and all other creatine-based products for ALS, after which Avicena plans to meet with the FDA.

"We will then propose our next steps to them," Tsao-Nivaggioli said, adding that that meeting could come late this year or early next year.

In the meantime, ALS-02's development is marching forward, with Avicena and the patient consortium planning a dose-escalation study to determine its optimal treatment dosage. Studies of the company's creatine-based therapeutics in other neurodegenerative diseases have suggested an improved response at higher doses without increasing adverse effects.

There are about 30,000 individuals with ALS in the U.S. at any given time; the progressive neurodegenerative disorder

is commonly called Lou Gehrig's disease. Right now, ALS patients have one FDA-approved treatment, Rilutek (riluzole, from Sanofi-Aventis Group). A glutamate inhibitor, it offers a survival benefit that lasts about 60 days. The disease has no known cure.

Among Avicena's other neurodegenerative disease programs is a Phase II compound for Huntington's, HD-02, which also has orphan drug designation. Phase I/II data on HD-02 showed that it increased serum and brain levels of creatine at a dose of 8 grams per day, and decreased the amount of serum 8-hydroxy-2'-deoxyguanosine, which is

markedly elevated in those patients. Also, another program is on the cusp of Phase III trial for Parkinson's.

Avicena's earlier-stage clinical programs are focused on diseases such as creatine transporter defect, Duchenne's muscular dystrophy and Charcot-Marie tooth syndrome.

Once a division within Repligen Corp., of Waltham, Mass., Avicena was incorporated as a solo entity in 1999. ■