Background: These are the results of a 24-week open-label (OL) extension period after a 24-week double-blind (DB) period of a Phase III study evaluating edaravone versus placebo in ALS patients (NCT01492686).

Hypothesis: To assess the efficacy and safety of an additional 24 weeks of edaravone (E-E) versus DB placebo switched to OL edaravone (P-E).

Methods: Patients entered DB with retained broad functionality (all ALSFRS-R individual item scores ≥2 points) and normal respiratory function (%FVC ≥80%) at baseline. DB completers could enter the OL period to receive active edaravone. OL consisted of an additional 6 cycles of 60-mg intravenous edaravone once-daily for 10 days within a 14 day period, followed by a 14-day drug-free period (28 days per cycle). The main efficacy endpoint was ALSFRS-R change across 12 cycles. Other endpoints included ALSAQ-40 scores and survival analyses for key ALS events (death and certain disease progression). Safety endpoints, including adverse events (AEs), were collected. The prespecified statistical plan called for descriptive statistics only.

Results: Of the 137 patients who entered 24-week DB, 123 patients entered 24-week OL; 65/123 (E-E) and 58/123 patients (P-E) were previously randomized to edaravone or placebo, respectively. In 24-week DB period, edaravone showed less decrease in ALSFRS-R compared with placebo (between-group difference 2.49±0.76 at 24 weeks, p=0.001). In 24-week OL period, E-E group showed less observed change from baseline in ALSFRS-R than P-E group (between-group difference 4.17±1.40 at 48 weeks) (adjusted mean). Edaravone improved ALSAQ-40 with a difference between edaravone and placebo in the 24-week DB period (8.79±4.03, p=0.031), and maintained the difference in the 24-week OL period (10.71±4.51 at 48 weeks) (adjusted mean). Death or events of certain disease progression occurred in 10 and 19 patients in the E-E and P-E groups, respectively. The most commonly reported AEs (≥5% of patients in both treatment groups) were nasopharyngitis, respiratory disorder, constipation, dysphagia, and contusion.

Conclusion: Based on findings of the open-label extension up to 48 weeks, early ALS phase intervention with edaravone may confer benefit to patients for whom treatment is promptly initiated versus individuals for whom treatment is delayed by 6 months.