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CYTOKINETICS ANNOUNCES COURAGE-ALS MET CRITERIA FOR FUTILITY AT SECOND INTERIM ANALYSIS

Company Plans to Discontinue the Phase 3 Clinical Trial of Reldesemtiv After Data Monitoring Committee Found No Effect on Primary or Key Secondary Endpoints

Cytokinetics announced that the Data Monitoring Committee (DMC) for COURAGE-ALS (**C**linical **O**utcomes **U**sing ***R****eldesemtiv* on **A**LSFRS-R in a **G**lobal **E**valuation in **ALS**), recently convened to conduct the second planned interim analysis of this Phase 3 clinical trial.

The DMC reviewed unblinded data from COURAGE-ALS and recommended the discontinuation of the clinical trial due to futility, as it found no evidence of effect in patients treated with *reldesemtiv* relative to placebo on the primary endpoint of change from baseline to 24 weeks in ALSFRS-R or in key secondary endpoints. Given these results, study conduct in COURAGE-ALS will be concluding. In addition, Cytokinetics plans to discontinue treatment with *reldesemtiv* in all patients including those in the open-label extension study, COURAGE-ALS OLE.

"We are extremely disappointed with this outcome and would like to thank the people with ALS, caregivers, investigators and clinical trial staff for their participation in COURAGE-ALS," said Robert I. Blum, Cytokinetics' CEO and President. "Cytokinetics has been committed to the ALS community for more than a decade and recognizes the urgency to bring new potential medicines to the forefront for this grievous disease. In the coming months, we will assess next steps relating to our neuromuscular development programs."

The second interim analysis was triggered 24 weeks after at least one third of the planned sample size was randomized in COURAGE-ALS. At the interim analysis, approximately 460 patients had been randomized and over 200 had reached the 24-week assessment of the trial endpoints. This interim analysis assessed the primary and key secondary endpoints for potential futility as well as provided for a potential fixed increase in total enrollment, if it had been deemed necessary to augment the statistical power of the trial, or to continue the trial to its conclusion as planned. Cytokinetics intends to notify all regulatory agencies and clinical trial investigators involved in COURAGE-ALS of these interim findings. The full data set from this trial is being analyzed and more details will be presented at an upcoming medical meeting.

COURAGE-ALS & COURAGE-ALS OLE: Trial Design

COURAGE-ALS was a Phase 3, multi-center, double-blind, randomized, placebo-controlled trial of *reldesemtiv* designed to enroll approximately 555 patients with ALS. Patients were randomized 2:1 to receive 300 mg of *reldesemtiv* or matching placebo dosed orally twice daily for 24 weeks, followed by a 24-week period in which all patients received 300 mg of *reldesemtiv* twice daily. Eligible patients were within the first two years of their first symptom of muscle weakness, had a vital capacity of ≥65% predicted, and a screening ALS Functional Rating Scale – Revised (ALSFRS-R) ≤44. Patients taking stable doses of *edaravone* and/or *riluzole* were permitted to enroll, and randomization was stratified accordingly. The primary efficacy endpoint was change from baseline to 24 weeks in ALSFRS-R. Secondary endpoints included combined assessment of ALSFRS-R total score, time to onset of respiratory insufficiency and survival time up to week 24 using a joint rank test; change from baseline to 24 weeks for vital capacity; ALSAQ-40; and bilateral handgrip strength. The trial included two planned unblinded interim analyses conducted by the Data Monitoring Committee. The first interim analysis assessed for futility, 12 weeks after approximately one-third or more of the planned sample size were randomized. The second interim analysis assessed for futility with the option for a fixed increase in total enrollment, if it had been deemed necessary, to augment the statistical power of the trial.

An open-label extension trial, COURAGE-ALS OLE, has enrolled people who completed participation in COURAGE-ALS. In COURAGE-ALS OLE, participants received 300 mg of *reldesemtiv* dosed orally twice daily for 48 weeks after which they were eligible to transition into the Managed Access Program, a program designed to provide access to *reldesemtiv* for patients diagnosed with ALS who have completed a prior Cytokinetics clinical trial with *reldesemtiv* or *tirasemtiv*.

Source: **press release Cytokinetics**