New Publication Shows Respiratory Decline Correlated With Disease Progression in People Living With ALS

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Retrospective Analyses of Clinical Trials in ALS Shows Faster Rate of Decline in Slow Vital Capacity Strongly Predicts Increased Risk of Future Clinical Events

SOUTH SAN FRANCISCO, Calif., Nov. 30, 2017 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq:CYTK) today announced the publication of retrospective analyses of data from controlled trials of patients with ALS, showing that the rate of decline in SVC strongly predicted meaningful clinical events, including time to respiratory insufficiency and death in patients with ALS. The publication, titled "Association Between Decline in Slow Vital Capacity and Respiratory Insufficiency, Use of Assisted Ventilation, Tracheostomy, or Death in Patients With Amyotrophic Lateral Sclerosis," was published in the *Journal of the American Medical Association (JAMA) Neurology*.

"These results suggest that respiratory function is an important prognostic indicator of clinical progression in people with ALS and adds to a growing body of literature on this correlation," said Fady I. Malik, MD, PhD, Cytokinetics' Executive Vice President of Research & Development. "Vital capacity is a key measure used by clinicians to measure disease progression during routine clinic visits and this analysis reinforces its use to guide critical clinical management decisions."

In this retrospective analysis, placebo data from each of EMPOWER, the Phase 3 clinical trial of *dexpramipexole* in ALS, BENEFIT-ALS, the Phase 2 clinical trial of *tirasemtiv* in ALS, and the Pooled Resource Open-Access ALS Clinical Trials (PRO-ACT) database were analyzed to investigate the natural history of respiratory function decline in patients with ALS, as measured by SVC. Additionally, data from EMPOWER were used to assess the relationship between SVC and respiratory-related clinical events. A total of 893 patients with ALS were included in the analysis, and were on average 56.7 years old, with an SVC of 90.4 percent predicted at baseline; 65.5 percent were male and 20.3 percent had bulbar-onset ALS.

The average slope of SVC decline was -2.73 percent/month in EMPOWER, -2.74 percent/month in BENEFIT-ALS, and -2.90 percent/month in PRO-ACT. In EMPOWER, two clinically relevant subgroups were associated with a faster rate of SVC decline: patients 65 years of age and older (-3.6 percent per month; p=0.005) and patients with a baseline ALSFRS-R score ≤39 (-3.1 percent per month, p=0.001). Statistically significant correlations were observed between change from baseline in percent predicted SVC and other respiratory measures including change from baseline in SNIP (r=0.38, p<0.001), and change from baseline in the individual items of the respiratory domain of the ALSFRS-R including dyspnea (r=0.23, p<0.001), orthopnea (r=0.23, p<0.001), and respiratory insufficiency (r=0.26, p<0.001). Additionally, a Cox proportional hazards regression model of time to clinical events showed that slowing the rate of SVC decline by 1.5 percentage points per month in the first six months reduced the risk of decline in any of the three ALSFRS-R respiratory subdomains or death by 19 percent, first onset of respiratory insufficiency or death by 22 percent, tracheostomy or death by 23 percent, and death by 23 percent (all p<0.001). The results of these analyses suggest that the rate of decline in SVC in patients with ALS correlates with the risk of clinically meaningful events, such as respiratory insufficiency or death in patients.

About ALS

ALS is a progressive neurodegenerative disease that afflicts approximately 30,000 people in the United States and a comparable number of patients in Europe. Approximately 6,000 new cases of ALS are diagnosed each year in the United States. The average life expectancy of an ALS patient is approximately three to five years after diagnosis and only approximately 10 percent of patients survive for more than 10 years. Death is usually due to respiratory failure because of diminished strength in the skeletal muscles responsible for breathing. Few treatment options exist for these patients, resulting in a high unmet need for new therapies to address functional deficits and disease progression.

About Vital Capacity and Disease Progression in ALS

Vital capacity is a measure used in the management of ALS to assess the strength of respiratory muscles and, as a predictor of disease progression and survival, is used in clinical practice to make intervention decisions. Vital capacity can be measured as slow vital capacity (SVC) or forced vital capacity (FVC). SVC may be easier to perform in patients with bulbar and advanced disease. Vital capacity measures the amount of air expelled from the lungs after a maximum inhalation and is used to assess the strength of the skeletal muscles responsible for breathing (e.g., the diaphragm). Vital capacity is often expressed in terms of the percentage of the normal value predicted for the individual patient's sex, age, and height; i.e., percent predicted vital capacity. Percent predicted vital capacity declines an average of 2-3 percentage points per month in patients with ALS and is the most frequently monitored measure of respiratory function to measure disease progression. Vital capacity is also used to inform critical clinical decisions, such as initiation of non-invasive ventilation, feeding tube placement and palliative care.

About Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators as potential treatments for debilitating diseases in which muscle performance is compromised and/or declining. As a leader in muscle biology and the mechanics of muscle performance, the company is developing small molecule drug candidates specifically engineered to increase muscle function and contractility. Cytokinetics is collaborating with Amgen Inc. ("Amgen") to develop *omecamtiv mecarbil*, a novel cardiac muscle activator. *Omecamtiv mecarbil* is the subject of GALACTIC-HF, an international Phase 3 clinical trial in patients with heart failure. Amgen holds an exclusive worldwide license to develop and commercialize *omecamtiv mecarbil* with a sublicense held by Servier for commercialization in Europe and certain other countries. Cytokinetics is collaborating with Astellas Pharma Inc. ("Astellas") to develop CK-2127107, a next-generation FSTA. CK-2127107 has been granted orphan drug designation by the FDA for the potential treatment of SMA. CK-2127107 is the subject of three ongoing Phase 2 clinical trials enrolling patients with spinal muscular atrophy, chronic obstructive pulmonary disease and ALS. Astellas is also conducting a Phase 1b clinical trial of CK-2127107 in elderly adults with limited mobility. Astellas holds an exclusive worldwide license to develop and commercialize CK-2127107. Licenses held by Amgen and Astellas are subject to Cytokinetics' specified co-development and co-commercialization rights. For additional information about Cytokinetics, visit www.cytokinetics.com.

Forward-Looking Statements

This press release contains forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995 (the "Act"). Cytokinetics disclaims any intent or obligation to update these forward-looking statements, and claims the protection of the Act's Safe Harbor for forward-looking

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