Cytokinetics Announces Oral Bioavailability Results for CK-1827452

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South San Francisco, CA, December 1, 2006 - Cytokinetics, Incorporated (Nasdaq: CYTK) announced today that the results from an oral bioavailability study evaluating CK-1827452, a novel cardiac myosin activator, in healthy volunteers support advancement of an oral formulation of CK-1827452 into Phase II clinical trials. The study was designed as an open-label, four way crossover study to investigate the absolute bioavailability, and the effects of food on the bioavailability, of two oral formulations of CK-1827452.

In this study, ten healthy volunteers were enrolled and received in random order CK-1827452 at 0.125 mg/kg administered: (i) as a reference intravenous infusion at a constant rate over one hour, (ii) as a liquid solution taken orally in a fasted state, (iii) as an immediate-release solid formulation taken orally in a fasted state, and (iv) as an immediate-release solid formulation taken orally following consumption of a standard, high-fat breakfast. Pharmacokinetic data from this study demonstrated absolute oral bioavailability of approximately 100% for each of the three conditions of oral administration.

These data suggest relatively little variability in oral absorption between patients and therefore predictable plasma levels with oral administration of CK-1827452, which may help to ensure the safety and tolerability of CK-1827452 during chronic oral administration. Oral absorption while fasting was rapid for the liquid solution and immediate-release solid formulation. The median time to maximum plasma concentration after dosing (Tmax) was 0.5 hours for the liquid solution and 1 hour for the immediate-release formulation. Food delayed the rate of absorption (median Tmax 3 hr), but did not diminish the extent of absorption. All four conditions of administration were well tolerated, and there were no serious adverse events.

The oral bioavailability data from this study suggests that absorption of CK-1827452 may have a low susceptibility for pharmacokinetic interactions with drugs metabolized by the cytochrome P450 enzymes in the liver and small intestine. These data also indicate that CK-1827452 is unlikely to interact pharmacokinetically with drugs that inhibit intestinal p-glycoprotein, a protein which acts to limit the absorption of some molecules by pumping them back into the intestinal lumen following their absorption into the epithelial cells of the small intestine. The rapid oral absorption of the immediate-release solid formulation under fasted conditions suggests that a modified-release formulation may be desirable for later-stage development and commercialization. Finally, analysis of the combined pharmacokinetic data from this oral bioavailability study and from the first-in-humans study (in which healthy volunteers received intravenous CK-1827452) supports dosing CK-1827452 both intravenously and orally without requiring adjustment for patient weight.

“We are pleased that this study demonstrated such high levels of bioavailability in humans for CK-1827452 when administered orally,” stated David J. Morgans, Jr., Ph.D, Cytokinetics' Senior Vice President of Preclinical Research and Development. “These data are consistent with what we had observed in preclinical models and will inform further formulation development and manufacturing activities in 2007.”

“We believe these data further support our Phase II clinical trials program for CK-1827452 that is planned to evaluate both oral and intravenous formulations and is designed to evaluate the pharmacokinetics and pharmacodynamic effects of this novel drug candidate in heart failure patients in the inpatient and outpatient treatment settings,” stated Andrew A. Wolff, M.D., F.A.C.C., Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer.

Development Status of CK-1827452

Data from the first-in-humans Phase I clinical trial of CK-1827452 administered intravenously were previously announced at the Heart Failure Society of America meeting in Seattle in September, 2006 and the American Heart Association Scientific Session in November, 2006. This clinical trial demonstrated that the maximum tolerated dose (MTD) was 0.5 mg/kg/hr for the six-hour infusion in healthy volunteers. At this dose, the six-hour infusion of CK-1827452 produced a mean increase in left ventricular ejection fraction of 6.8 absolute percentage points as compared to placebo (p