

BIO WORLD[®] TODAY

TUESDAY
MARCH 25, 2008

THE DAILY BIOTECHNOLOGY NEWSPAPER

VOLUME 19, No. 58
SPECIAL REPRINT

Cytokinetics Sees Shares Rise on Positive Heart Drug Data

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Cytokinetics Inc. said interim findings from a Phase IIa study of its drug candidate for heart failure patients, CK-1827452, showed that it was well tolerated and improved heart pumping function.

The product, a cardiac myosin activator, is being studied as a potential treatment for two different types of heart failure patients.

An intravenous form of the drug is being studied as a potential treatment for patients who require hospitalization due to acutely decompensated heart failure. A pill form of the drug would be for outpatients with chronic heart failure.

In the ongoing Phase IIa study, CK-1827452 demonstrated statistically significant increases in indices of cardiac ventricular function, the South San Francisco-based company said. News of the positive findings sent shares of Cytokinetics (NASDAQ:CYTK) up 10 cents or 2.9 percent, closing at \$3.50.

Michael Aberman, analyst with Credit Suisse, wrote in a research note, "These data are in-line with our expectations and represent an important milestone for CK-452 as they confirm pharmacodynamic activity in the target heart failure population."

In rating the company an "outperform," he said, "CK-452 could be the first heart failure drug to increase cardiac output without increasing oxygen consumption. We are also comforted by the lack of serious adverse events, which were seen in the Phase I trial, which suggests that the drug has a manageable therapeutic window."

This is the first clinical validation that the product behaves "exactly as we would have predicted" in heart failure patients, based on prior observations in animal studies and in healthy volunteers, Robert I. Blum, president and CEO at Cytokinetics, told *BioWorld Today*.

Top-line results from the trial will be reviewed at an investor breakfast in Chicago March 31. Data from the first two cohorts of the trial will be presented at the Heart Failure Congress, an annual meeting of the Heart Failure

Association of the European Society of Cardiology, in Milan, Italy, in June.

In the study, CK-1827452, was administered as an intravenous infusion to two cohorts of eight patients each. Each patient was given two hours of dosing during four visits, with one placebo given at one of the visits, which were spaced at least a week apart. The dosing was tied to plasma concentrations.

The patients in the study were not acutely ill, but over the long term, heart failure can lead to frequent hospitalizations or even death, Blum explained.

CK-1827452 may improve on current treatments such as diuretics, beta-blockers and ace inhibitors, Blum said, adding that such treatments are aimed at correcting the body's maladaptive responses to heart failure, which cause the body to increase blood pressure and hold onto excess fluids.

While there are interventions available for these problems, current treatments don't improve pumping function over the long term, he said.

When compared to placebo, CK-1827452 produced statistically significant and clinically relevant increases in Doppler-derived stroke volume and fractional shortening in association with statistically significant prolongations of systolic ejection time, according to the company.

Statistically significant correlations were observed between the increases in each of the three indices of cardiac ventricular function and increases in the plasma concentration of CK-1827452, the company news release said.

Left ventricular ejection fraction, a measurement with high variability in patients with ventricular disease, also increased with ascending plasma concentrations.

However, that increase in left ventricular systolic function did not reach statistical significance in those initial cohorts.

Heart rate and blood pressure remained unchanged in the first two cohorts of the Phase IIa trial, and the interim

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safety data suggested that the drug candidate is well tolerated, the company said.

A third cohort of the study has been initiated, with longer I.V. infusion of 24 hours, compared to two hours in the first two cohorts, Andrew Wolff, chief medical officer at Cytokinetics, told *BioWorld Today*.

Additional Phase IIa studies also are planned later this year.

A catheterization lab study is expected to enroll similar patients to the ongoing study and another Phase II a study will involve the largest subset of heart failure patients, those with ischemic myocardial cardiomyopathy, in which the heart does not pump well enough due to damage from coronary artery disease and prior heart attack.

Cytokinetics is collaborating with Amgen Inc., of Thousand Oaks, Calif., on developing the product candidate.

The company also has three programs in oncology, including ispinesib (SB-715992), which is in Phase II for breast cancer and various other cancers; SB-743921, which is in Phase I/II for non-Hodgkin's lymphoma; and GSK-923295, which is expected to enter Phase I studies in 2007.

All three products are part of a collaboration with London-based GlaxoSmithKline plc, originally signed in June 2001.

The alliance is focused on therapies that target KSP – kinesin spindle protein – and other cytoskeletal proteins involved in cell proliferation. ■