UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

# FORM 8-K

## CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): December 18, 2008

# Cytokinetics, Incorporated

(Exact name of registrant as specified in its charter)

| Delaware | 000-50633 | 94-3291317 |
|---|---|---|
| (State or other jurisdiction of incorporation) | (Commission File Number) | (I.R.S. Employer Identification No.) |
| 280 East Grand Avenue, South San Francisco, California | | 94080 |
| (Address of principal executive offices) | | (Zip Code) |

Registrant's telephone number, including area code: (650) 624 - 3000

Not Applicable

Former name or former address, if changed since last report

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

[ ] Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
[ ] Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
[ ] Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
[ ] Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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**Item 8.01 Other Events.**

On December 18, 2008, Cytokinetics, Incorporated issued a press release announcing top-line results from a Phase IIa clinical trial evaluating the safety of CK-1827452 in patients with ischemic cardiomyopathy and angina. Cytokinetics also announced that it anticipates that in early 2009 it will complete the delivery of the clinical data required to inform the potential exercise of Amgen Inc.'s option under the companies' strategic alliance. CK-1827452 is a novel cardiac myosin activator and the subject of a collaboration and option agreement between Cytokinetics and Amgen Inc. This novel drug candidate is being developed in both intravenous and oral formulations for the potential treatment of patients hospitalized for heart failure and outpatients with chronic heart failure. A copy of the press release is filed as Exhibit 99.1 to this Current Report on Form 8-K, and is incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

The following Exhibit is filed as part of this Current Report on Form 8-K:

Exhibit No. Description
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99.1 Press release, dated December 18, 2008.

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Cytokinetics, Incorporated

*December 18, 2008*

*By: Sharon Barbari*

*Name: Sharon Barbari*
*Title: Senior Vice President, Finance and Chief Financial Officer*

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Exhibit Index

| Exhibit No. | Description |
| --- | --- |
| 99.1 | Press Release, dated December 18, 2008 |

Contact:
*Christopher S. Keenan*
*Director, Investor Relations*
*(650) 624-3000*

**CYTOKINETICS ANNOUNCES PHASE IIA CLINICAL TRIAL RESULTS RELATING TO CK-1827452 IN PATIENTS WITH ISCHEMIC CARDIOMYOPATHY AND ANGINA**

***Safety Data Support Progression to Phase IIb Development Program***

***Update on Amgen Option and CK-1827452 Clinical Trials Program***

***South San Francisco, CA, December 18, 2008 –*** Cytokinetics, Incorporated (Nasdaq: CYTK) announced today top-line results from a Phase IIa clinical trial evaluating the safety of CK-1827452 in patients with ischemic cardiomyopathy and angina. The primary safety endpoint was defined as stopping an exercise test during treatment with CK-1827452 (versus placebo) due to unacceptable angina at an earlier exercise stage than at baseline. This endpoint was observed in one patient receiving placebo and did not occur in any patient receiving CK-1827452.

"We are pleased with these clinical trial results of CK-1827452 in patients with angina and ischemic cardiomyopathy, as we believe they support further study of the drug candidate in higher-risk patients with heart failure. We look forward to presenting the complete set of data from this trial at an appropriate scientific and medical forum in 2009," stated Andrew A. Wolff, M.D., F.A.C.C., Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "Based on the data from this trial, together with pharmacokinetic and pharmacodynamic data from other recent trials of CK-1827452, we intend to initiate in mid-2009 a Phase IIb clinical development program in patients hospitalized for heart failure and higher-risk chronic heart failure outpatients. This Phase IIb program will be designed to select appropriate dose regimens for clinical endpoint-driven trials to support potential registration."

CK-1827452 is a novel cardiac myosin activator and the subject of a collaboration and option agreement between Cytokinetics and Amgen Inc. This novel drug candidate is being developed in both intravenous and oral formulations for the potential treatment of patients hospitalized for heart failure and outpatients with chronic heart failure. Cytokinetics announced today that it anticipates that in early 2009 it will complete the delivery of the clinical data required to inform the potential exercise of Amgen's option under the companies' strategic alliance.

Phase IIa Clinical Trial of CK-1827452 in Patients with Ischemic Cardiomyopathy and Angina

This double-blind, randomized, placebo-controlled Phase IIa clinical trial was designed to evaluate both intravenous and oral formulations of CK-1827452 in patients with ischemic cardiomyopathy and angina. The primary objective of this trial was to assess the effect of intravenous CK-1827452 on symptom-limited treadmill exercise tolerance in this patient population. The secondary objective of this trial was to assess the tolerability and resulting plasma concentrations of CK-1827452 administered as an oral formulation. The trial was designed to evaluate two cohorts of 45 patients each with ischemic cardiomyopathy and angina who have an ejection fraction of less than or equal to 35 percent. During screening, patients underwent two symptom-limited exercise treadmill tests (ETTs); the shorter of these two ETTs was defined as the baseline. Eligible patients in each cohort were then randomized to receive a two-hour double-blind intravenous loading infusion of CK-1827452 (or placebo) followed by an eighteen-hour double-blind intravenous maintenance infusion of CK-1827452 (or placebo). A third ETT (ETT3) was performed during the final two hours of the maintenance infusion. In each cohort, patients whose symptom-limited exercise tolerance during the infusion did not deteriorate relative to baseline received either CK-1827452 or placebo administered orally for seven days. CK-1827452 plasma levels were measured during the infusions, as well as before and one hour after the final oral dose.

Patients in the first cohort were randomized in a 2-to-1 ratio to CK-1827452 at a dose level intended to target a maximum plasma concentration of 295 ng/ml during the infusion and 184 ng/ml during oral dosing or to placebo. Patients in the second cohort were randomized in a 2-to-1 ratio to CK-1827452 at a dose level intended to target a plasma concentration of 550 ng/ml during the infusion and 368 ng/ml during oral dosing or to placebo.

A total of 94 patients were enrolled and treated in this Phase IIa clinical trial; 29 patients received placebo, 31 received CK-1827452 at the lower dose level, and 34 received CK-1827452 at the higher dose level. The primary safety endpoint was defined as stopping exercise during the third ETT due to unacceptable angina and at an exercise stage earlier than at baseline. This endpoint was observed in one patient receiving placebo and did not occur in any patient receiving CK-1827452 at either dose level.

The majority of unique adverse events (21 of 27) in the trial were classified as mild in severity; 4 were classified as moderate and 2 were reported as severe. Of the 94 patients treated, 19 reported at least one unique adverse event at any time during the trial: 5 patients on placebo; 2 patients on the lower dose level of CK-1827452; and 12 patients on the higher dose level of CK-1827452, who reported a total of 18 unique adverse events (15 of which were classified as mild in severity).

The 2 severe adverse events were the only two serious adverse events reported; both occurred in the same patient, who received intravenous CK-1827452 in Cohort 2. This patient, who stopped one of his screening ETTs for unacceptable angina, tolerated the infusion of CK-1827452 while at rest uneventfully but developed unacceptable angina during ETT3 which persisted for several minutes into the recovery period. Cardiac catheterization was performed, identifying a severe stenosis of the proximal left anterior descending coronary artery that necessitated treatment with a coronary stent. The investigator reported two serious adverse events in this patient: an acute coronary syndrome, relating to the persistent angina after ETT3, and a post-procedural myocardial infarction, relating to elevations in troponin I (but not creatine kinase-MB) which occurred only after placement of the coronary stent. Both these events were judged by the investigator to have been unrelated to treatment with the study drug.

Update on Phase IIa Clinical Trial of CK-1827452 in Patients with Stable Heart Failure

Cytokinetics also provided today an update on another Phase IIa clinical trial. This clinical trial is a multi-center, double-blind, randomized, placebo-controlled, dose-escalation, pharmacokinetic and pharmacodynamic trial of CK-1827452 administered intravenously to patients with stable heart failure. The primary objective of this trial is to evaluate the safety and tolerability of CK-1827452 administered as an intravenous infusion to stable heart failure patients. The secondary objectives of this trial are to establish a relationship between the plasma concentration and pharmacodynamic effects of CK-1827452 and to determine the pharmacokinetics of CK-1827452 in stable heart failure patients. In addition to routine assessments of vital signs, blood sampling for CK-1827452 levels, and electrocardiographic monitoring, echocardiograms are performed to evaluate cardiac function at various pre-defined time points before, during, and after the infusion of CK-1827452.

In this trial, CK-1827452 is administered as an intravenous infusion to cohorts of eight patients each. In Cohorts 1 through 4, patients underwent four treatment periods, receiving three escalating active doses of CK-1827452 and one placebo treatment randomized into the dose escalation sequence to

maintain blinding. Patients receive a loading infusion to rapidly achieve a target plasma concentration of CK-1827452 during the first hour, followed by slower infusions intended to maintain that plasma concentration during the remainder of treatment. The first two of these cohorts were designed to study a range of target CK-1827452 plasma concentrations, from 90 ng/ml in the lowest dose regimen in Cohort 1 to 650 ng/ml in the highest dose regimen in Cohort 2; Cohorts 3 through 5 were designed to gain experience across the same range of plasma concentrations, but with infusion durations of 24 hours in Cohorts 3 and 4 and 72 hours in Cohort 5.

In November 2008, Cytokinetics reported interim results from this ongoing Phase IIa clinical trial. These interim analyses demonstrated statistically significant increases in systolic ejection time ($p < 0.0001$) and fractional shortening ($p < 0.05$) at CK-1827452 plasma concentrations greater than 100 ng/mL, statistically significant increases in stroke volume ($p < 0.01$) at CK-1827452 plasma concentrations greater than 200 ng/mL, and statistically significant increases in ejection fraction ($p < 0.05$) at CK-1827452 plasma concentrations greater than 300 ng/mL,. In addition, there were statistically significant correlations between increasing CK-1827452 plasma concentration and increases in systolic ejection time, stroke volume, and fractional shortening (all $p < 0.0001$), ejection fraction ($p < 0.0005$) and cardiac output ($p < 0.01$). There were also statistically significant correlations between increasing CK-1827452 concentration and decreases in supine and standing heart rate (both $p < 0.0001$) and left ventricular end-systolic volume ($p < 0.05$).

Dosing in Cohort 4 has been completed. In addition, 4 patients have completed dosing in Cohort 5; furthermore, sufficient patients now have been enrolled in this cohort such that Cytokinetics anticipates the completion of dosing in January 2009. Final data from this clinical trial are expected to be presented at an appropriate scientific and medical forum in 2009.

Phase I Clinical Trial Update for CK-1827452

Cytokinetics also provided an update on a recently completed Phase I clinical trial designed to evaluate the potential for certain drug-drug interactions. This clinical trial was a single-center, open-label, sequential, parallel group study in healthy male subjects to evaluate the potential for certain drug-drug interactions. The primary objective of this study was to evaluate the effect of *ketoconazole* (a potent inhibitor of the drug-metabolizing enzyme, cytochrome P450 (CYP3A4)) at steady-state on the pharmacokinetics of a single oral dose of CK-1827452 in subjects who are either extensive metabolizers (EM) or poor metabolizers (PM) with respect to their defined genotype for the drug-metabolizing enzyme CYP2D6. The secondary objectives were to evaluate the pharmacokinetic parameters of CK-1827452 administered alone in subjects with PM genotype for CYP2D6 as compared to subjects with EM genotype for CYP2D6 and to evaluate the effect of *diltiazem* (a moderate inhibitor of CYP3A4) at steady-state in subjects with the EM genotype for CYP2D6 if there was evidence of any significant pharmacokinetic interaction between *ketoconazole* and CK-1827452.

There were no clinically important differences observed between EM and PM subjects; furthermore, no clinically meaningful drug-drug interactions with either *ketoconazole* or *diltiazem* were identified in either EM or PM subjects.

**Development Status of CK-1827452**

In addition to these the two above-mentioned Phase IIa clinical trials of CK-1827452, in April 2008, Cytokinetics opened enrollment in an open-label, non-randomized Phase IIa clinical trial designed to evaluate an intravenous formulation of CK-1827452 administered to patients with stable heart failure undergoing clinically indicated coronary angiography in a cardiac catheterization laboratory. Results from this ongoing trial are expected in 2009. In addition to the above-mentioned Phase I clinical trial of CK-1827452, Cytokinetics has completed four other Phase I clinical trials of CK-1827452 in healthy subjects: a first-time-in-humans study evaluating an intravenous formulation, an oral bioavailability study evaluating both intravenous and oral formulations, and two studies of oral formulations: a dose proportionality study and a study evaluating modified-release formulations. Data from each of these trials have been reported previously.

**Background on Cardiac Myosin Activators and Cardiac Contractility**

Cardiac myosin is the cytoskeletal motor protein in the cardiac muscle cell that is directly responsible for converting chemical energy into the mechanical force resulting in cardiac contraction. Cardiac contractility is driven by the cardiac sarcomere, a highly ordered cytoskeletal structure composed of cardiac myosin, actin and a set of regulatory proteins, and is the fundamental unit of muscle contraction in the heart. The sarcomere represents one of the most thoroughly characterized protein machines in human biology. Cytokinetics' cardiovascular program is focused towards the discovery and development of small molecule cardiac myosin activators in order to create next-generation treatments to manage acute and chronic heart failure. Cytokinetics' program is based on the hypothesis that activators of cardiac myosin may address certain mechanistic liabilities of existing positive inotropic agents by increasing cardiac contractility without increasing intracellular calcium. Current inotropic agents, such as beta-adrenergic receptor agonists or inhibitors of phosphodiesterase activity, increase cardiac cell contractility by increasing the concentration of intracellular calcium, which further activates the cardiac sarcomere; this effect on calcium levels, however, also has been linked to potentially life-threatening side effects. The inotropic mechanism of current drugs also increases the velocity of cardiac contractility and shortens systolic ejection time. In contrast, cardiac myosin activators have been shown to work in the absence of changes in intracellular calcium by a novel mechanism that directly stimulates the activity of the cardiac myosin motor protein. Cardiac myosin activators accelerate the rate-limiting step of the myosin enzymatic cycle and shift the enzymatic cycle in favor of the force-producing state. This inotropic mechanism results not in an increase in the velocity of cardiac contraction, but instead, in a lengthening of the systolic ejection time, which results in increased cardiac contractility and cardiac output in a potentially more oxygen-efficient manner.

**About Cytokinetics**

Cytokinetics is a biopharmaceutical company focused on the discovery, development and commercialization of novel small molecule drugs that may address areas of significant unmet clinical needs. Cytokinetics' cardiovascular disease program is focused to cardiac myosin, a motor protein essential to cardiac muscle contraction. Cytokinetics' lead compound from this program, CK-1827452, a novel small molecule cardiac myosin activator, entered Phase II clinical trials for the treatment of heart failure in 2007. Under a strategic alliance established in 2006, Cytokinetics and Amgen Inc. are performing joint research focused on identifying and characterizing activators of cardiac myosin as back-up and follow-on potential drug candidates to CK-1827452. Amgen has obtained an option for an exclusive license to develop and commercialize CK-1827452, subject to Cytokinetics' development and commercial participation rights. Cytokinetics' cancer program is focused on mitotic kinesins, a family of motor proteins essential to cell division. Under a strategic alliance established in 2001, Cytokinetics and GlaxoSmithKline (GSK) are conducting research and development activities focused on the potential treatment of cancer. Cytokinetics is developing two novel drug candidates that have arisen from this program, *ispinesib* and SB-743921, each a novel inhibitor of kinesin spindle protein (KSP), a mitotic kinesin. GSK has an option for the joint development and commercialization of *ispinesib* and SB-743921. GSK-923295, an inhibitor of centromere-associated protein E (CENP-E) inhibitor, is being developed under the strategic alliance by GSK; GSK began a Phase I clinical trial with GSK-923295 in 2007. In April 2008, Cytokinetics announced the selection of a potential drug candidate directed towards skeletal muscle contractility which may be developed as a potential treatment for skeletal muscle weakness associated with neuromuscular diseases or other conditions. All of these drug candidates and potential drug candidates have arisen from Cytokinetics' research activities and are directed towards the cytoskeleton. The cytoskeleton is a complex biological infrastructure that plays a fundamental role within every human cell. Additional information about Cytokinetics can be obtained at www.cytokinetics.com.

*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 statements. Examples of such statements include, but are not limited to, statements relating to Cytokinetics' and its partners' research and development programs, including the initiation, design, enrollment, conduct, and results of clinical trials relating to CK-1827452 and the significance of such results; the planned progression of CK-1827452 into a Phase IIb clinical development program, and the timing of such progression; planned presentations and availability of clinical trial data relating to CK-1827452; Cytokinetics' provision of the required clinical data from its CK-1827452 Phase IIa clinical trials program to Amgen; and the properties and potential benefits of CK-1827452 and Cytokinetics' other drug candidates and potential drug candidates. Such statements are based on management's current expectations, but actual results may differ materially due to various risks and uncertainties, including, but not limited to, potential difficulties or delays in the development, testing, regulatory approvals for trial commencement, progression or product sale or manufacturing, or production of CK-1827452 or Cytokinetics' other drug candidates that could slow or prevent clinical development or product approval, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trials results, patient enrollment for or conduct of clinical trials may be difficult or delayed, including without limitation, due to political instability in countries where clinical trials of CK-1827452 or Cytokinetics' other drug candidates are being conducted, CK-1827452 or Cytokinetics' other drug candidates may have adverse side effects or inadequate therapeutic efficacy, the U.S. Food and Drug Administration or foreign regulatory agencies may delay or limit Cytokinetics' or its partners' ability to conduct clinical trials, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Amgen may elect not to exercise its option with respect to CK-1827452; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products; standards of care may change rendering CK-1827452 and Cytokinetics' other drug candidates obsolete; others may introduce products or alternative therapies for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from its partners, including option fees, milestones and royalties on future potential product sales under Cytokinetics' collaboration agreements with such partners. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission.*