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): May 23, 2022

Cytokinetics, Incorporated
(Exact Name of Registrant as Specified in Charter)

Delaware	**000-50633**	**94-3291317**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification Number)

350 Oyster Point Boulevard, South San Francisco, California 94080
(Address of Principal Executive Offices) (Zip Code)

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

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))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001	**CYTK**	**The Nasdaq Stock Market LLC**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events.

Today, May 23, 2022, Cytokinetics, Incorporated (the "Company" or "Cytokinetics") announced positive data relating to *aficamten* from REDWOOD-HCM OLE (**R**andomized **E**valuation of **D**osing **W**ith CK-274 in **O**bstructive **O**utflow **D**isease in **HCM O**pen **L**abel **E**xtension) and the results from two additional analyses of *omecamtiv mecarbil* from GALACTIC-HF (**G**lobal **A**pproach to **L**owering **A**dverse **C**ardiac Outcomes **T**hrough **I**mproving **C**ontractility in **H**eart **F**ailure), all presented in Late-Breaking Science Sessions at Heart Failure 2022, an International Congress of the European Society of Cardiology. The analysis from GALACTIC-HF related to low blood pressure has been simultaneously published in the *European Heart Journal*.

REDWOOD-HCM OLE: First Long-Term Data from Open Label Extension

Ahmad Masri, M.D., Assistant Professor of Medicine, Division of Cardiovascular Medicine, School of Medicine, Oregon Health & Science University, presented the first long-term data from REDWOOD-HCM OLE. Patients enrolled in REDWOOD-HCM OLE have completed participation in REDWOOD-HCM, the Phase 2 clinical trial of *aficamten*. The primary endpoint is the incidence of adverse events and left ventricular ejection fraction (LVEF) <50%. Secondary endpoints include measures of the long-term effects of *aficamten* on left ventricular outflow tract gradient (LVOT-G), and assessments of steady state pharmacokinetics. The trial also includes a cardiac magnetic resonance imaging sub-study to assess changes in cardiac morphology, function and fibrosis. All enrolled patients receive *aficamten*. After entry into REDWOOD-HCM OLE, each patient started at 5 mg once daily and underwent echocardiography-guided dose titration approximately every two weeks during the first six weeks and subsequently will continue to have study visits approximately every twelve weeks thereafter.

Data from 38 patients enrolled in REDWOOD-HCM OLE were presented today, including 30 patients treated for 12 weeks and 19 patients treated for 24 weeks. The data showed that treatment with *aficamten* was associated with substantial reductions in the average resting LVOT-G (mean change from baseline (SD) = -32.6 (28) mmHg, $p<0.0001$ at 12 weeks, -32.8 (32.3) mmHg, $p=0.0003$ at 24 weeks) and Valsalva LVOT-G (-42.7 (38.7) mmHg, $p<0.0001$ at 12 weeks, -51.1 (35.3) mmHg, $p<0.0001$ at 24 weeks). These reductions started to occur within two weeks of treatment, were sustained through 24 weeks of treatment, and were achieved with only modest decreases in the average LVEF (-3.2 (4.2) %, $p=0.0038$ at 24 weeks). Compared to baseline (47% Class II, 53% Class III), New York Heart Association (NYHA) Functional Class was improved in the majority of patients ($p<0.0001$ for improvement by one or more NYHA class), and no patients had a worsening of NYHA Class. At 12 weeks, 72% of patients improved by one class and 7% improved by two classes; at 24 weeks 61% of patients improved by one class and 17% improved by two classes. For patients reaching Week 24, 56% were Class I and 39% were Class II. There were also significant improvements in cardiac biomarkers including NTpro-BNP (reduction of 70% from baseline, $p<0.001$) and cardiac troponin (20% reduction, $p=0.002$). Treatment with *aficamten* was well-tolerated with one temporary discontinuation due to LVEF <50% and one temporary down-titration, neither related to drug. Both patients remain on treatment with *aficamten.*

GALACTIC-HF: Patients with Low Blood Pressure Treated with *Omecamtiv Mecarbil* Have an Increased Treatment Effect

Marco Metra, M.D., Professor of Cardiology & Director of the Institute of Cardiology, Department of Medical & Surgical Specialties, Radiological Sciences & Public Health, University & Civil Hospitals of Brescia, Italy presented an analysis from GALACTIC-HF on the effect of treatment with *omecamtiv mecarbil* in patients with HFrEF and low blood pressure. Of 8,232 patients with available baseline data on blood pressure, 1,473 patients (17.9%) had low systolic blood pressure defined as ≤100 mmHg. All patients with low blood pressure had an increased risk of cardiovascular death or heart failure events compared to patients without low blood pressure. In patients with low blood pressure, there was a greater treatment effect from *omecamtiv mecarbil* on the primary composite endpoint of cardiovascular death or first heart failure event than in patients without low blood pressure such that there was an absolute risk reduction of 9.8 events per 100 patient-years (hazard ratio, 0.81; 95% confidence interval [CI] 0.70, 0.94; interaction $p=0.051$). Patients with low blood pressure treated with *omecamtiv mecarbil* also experienced improvements in blood pressure over time as did those treated with placebo. Additionally, the incidence of treatment-emergent serious adverse events in patients with low blood pressure who received *omecamtiv mecarbil* (RR 0.88; 95% CI 0.82, 0.95; $p<0.001$) and adjudicated first stroke (RR 0.31; 95% CI 0.12, 0.79; $p=0.009$) was lower compared to placebo. Other measures of safety and tolerability were also similar between patients with low blood pressure and those without low blood pressure.

GALACTIC-HF: Treatment Effect of *Omecamtiv Mecarbil* on Primary Outcome Consistent in Patients with or without Tricuspid Regurgitation

Marianna Adamo, M.D., Interventional Cardiologist, University of Brescia, Italy presented an analysis from GALACTIC-HF on the impact of tricuspid regurgitation (TR) on the effectiveness of *omecamtiv mecarbil*. Of 8,256 patients in GALACTIC, 8,180 patients had data reported on TR, of which 6,476 (79%) had no TR, 919 (11%) had mild TR, and 785 (10%) had moderate/severe TR. Compared to patients with no TR, patients with moderate/severe TR were older ($p=0.003$), more often enrolled in an inpatient setting ($p<0.001$), had higher incidence of atrial fibrillation or flutter ($p<0.001$), were a worse NYHA functional class ($p<0.001$), had higher heart rate ($p<0.001$), and had worse cardiac biomarker levels including higher NT-proBNP and higher cardiac troponin ($p<0.001$ for both). Baseline moderate/severe TR was also associated with lower KCCQ Total Symptom Scores, an indicator of lower quality of life. Patients with moderate/severe TR in GALACTIC-HF experienced higher rates of the primary composite endpoint, cardiovascular death, all-cause death and heart failure events. The impact of moderate/severe TR on heart failure events was more pronounced in outpatients and in patients with higher LVEF, lower NT-proBNP and lower eGFR. The treatment effect of *omecamtiv mecarbil* on the primary outcome was consistent across patients with no TR, mild TR and moderate/severe TR such that baseline TR did not modify the treatment effect (interaction $p=0.91$).

About *Aficamten*

Aficamten is an investigational selective, small molecule cardiac myosin inhibitor discovered following an extensive chemical optimization program that was conducted with careful attention to therapeutic index and pharmacokinetic properties and as may translate into next-in-class potential in clinical development. *Aficamten* was designed to reduce the number of active actin-myosin cross bridges during each cardiac cycle and consequently suppress the myocardial hypercontractility that is associated with hypertrophic cardiomyopathy (HCM). In preclinical models, *aficamten* reduced myocardial contractility by binding directly to cardiac myosin at a distinct and selective allosteric binding site, thereby preventing myosin from entering a force producing state. The development program for *aficamten* is assessing its potential as a treatment that improves exercise capacity and relieves symptoms in patients with HCM as well as its long-term effects on cardiac structure and function. *Aficamten* received Breakthrough Therapy Designation for the treatment of symptomatic obstructive HCM from the U.S. Food & Drug Administration (FDA) as well as the National Medical Products Administration (NMPA) in China.

About Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a disease in which the heart muscle (myocardium) becomes abnormally thick (hypertrophied). The thickening of cardiac muscle leads to the inside of the left ventricle becoming smaller and stiffer, and thus the ventricle becomes less able to relax and fill with blood. This ultimately limits the heart's pumping function, resulting in symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity. A subset of patients with HCM are at high risk of progressive disease which can lead to atrial fibrillation, stroke and death due to arrhythmias. There are no FDA approved medical treatments that directly address the hypercontractility that underlies HCM.

About *Omecamtiv Mecarbil*

Omecamtiv mecarbil is an investigational, selective, small molecule cardiac myosin activator, the first of a novel class of myotropes[1] designed to directly target the contractile mechanisms of the heart, binding to and recruiting more cardiac myosin heads to interact with actin during systole. *Omecamtiv mecarbil* is designed to increase the number of active actin-myosin cross bridges during each cardiac cycle and consequently augment the impaired contractility that is associated with heart failure with reduced ejection fraction (HFrEF). Preclinical research has shown that *omecamtiv mecarbil* increases cardiac contractility without increasing intracellular myocyte calcium concentrations or myocardial oxygen consumption.[2-4]

The development program for *omecamtiv mecarbil* is assessing its potential for the treatment of HFrEF. Positive results from GALACTIC-HF, the first Phase 3 clinical trial of *omecamtiv mecarbil* demonstrated a statistically significant effect of treatment with *omecamtiv mecarbil* to reduce risk of the primary composite endpoint of cardiovascular (CV) death or heart failure events (heart failure hospitalization and other urgent treatment for heart failure) compared to placebo in patients treated with standard of care. No reduction in the secondary endpoint of time to CV death was observed. Adverse events and treatment discontinuation of study drug were balanced between treatment arms.

About Heart Failure

Heart failure is a grievous condition that affects more than 64 million people worldwide[5] about half of whom have reduced left ventricular function.[6,7] It is the leading cause of hospitalization and readmission in people age 65 and older.[8,9] Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor.[10] An estimated one in five people over the age of 40 are at risk of developing heart failure, and approximately 50 percent of people diagnosed with heart failure will die within five years of initial hospitalization.[11,12] More than 2 million people in the U.S. are estimated to have an ejection fraction <30%, indicating they may have severe heart failure.[13]

About Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and next-in-class muscle inhibitors as potential treatments for debilitating diseases in which muscle performance is compromised. As a leader in muscle biology and the mechanics of muscle performance, the company is developing small molecule drug candidates specifically engineered to impact muscle function and contractility. Cytokinetics is readying for the potential commercialization of *omecamtiv mecarbil*, its cardiac muscle activator, following positive results from GALACTIC-HF, a large, international Phase 3 clinical trial in patients with heart failure. Cytokinetics is also developing *aficamten*, a next-generation cardiac myosin inhibitor, currently the subject of SEQUOIA-HCM, the Phase 3 clinical trial of *aficamten* in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). *Aficamten* is also being evaluated in non-obstructive HCM in Cohort 4 of the Phase 2 clinical trial, REDWOOD-HCM. Cytokinetics is also developing *reldesemtiv*, an investigational fast skeletal muscle troponin activator, currently the subject of COURAGE-ALS, a Phase 3 clinical trial in patients with amyotrophic lateral sclerosis (ALS). Cytokinetics continues its over 20-year history of pioneering innovation in muscle biology and related pharmacology focused to diseases of muscle dysfunction and conditions of muscle weakness.

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 statements. Examples of such statements include, but are not limited to, statements relating to any of our other clinical trials, including statements relating to the potential benefits of *aficamten* for patients with obstructive hypertrophic cardiomyopathy and statements relating to the potential benefits of *omecamtiv mecarbil* for patients with heart failure with reduced ejection fraction. 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 Cytokinetics' drug candidates that could slow or prevent clinical development or product approval; Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy; the FDA or foreign regulatory agencies may delay or limit Cytokinetics' ability to conduct clinical trials; Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; standards of care may change, rendering Cytokinetics' drug candidates obsolete; and competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission.

References:

1. Psotka MA, Gottlieb SS, Francis GS et al. Cardiac Calcitropes, Myotropes, and Mitotropes. *JACC*. 2019; 73:2345-53.
2. Planelles-Herrero VJ, Hartman JJ, Robert-Paganin J. et al. Mechanistic and structural basis for activation of cardiac myosin force production by omecamtiv mecarbil. *Nat Commun*. 2017;8:190.
3. Shen YT, Malik FI, Zhao X, et al. Improvement of cardiac function by a cardiac myosin activator in conscious dogs with systolic heart failure. *Circ Heart Fail*. 2010; 3: 522-27.
4. Malik FI, Hartman JJ, Elias KA, Morgan BP, Rodriguez H, Brejc K, Anderson RL, Sueoka SH, Lee KH, Finer JT, Sakowicz R. Cardiac myosin activation: a potential therapeutic approach for systolic heart failure. *Science*. 2011 Mar 18;331(6023):1439-43.
5. James et al. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. *Lancet* 2018; 392: 1789–858.
6. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;128:e240-e327.
7. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016;37:2129–2200.
8. Roger VL. Epidemiology of Heart Failure. *Circulation Research*. 2013;113:646-659, originally published August 29, 2013. Doi: 10.1161/CIRCRESAHA.113.300268.
9. Kilgore M, Patel HK, Kielhorn A et al. Economic burden of hospitalizations of Medicare beneficiaries with heart failure. *Risk Manag Healthc Policy*. 2017; 10: 63-70.
10. Jhund PS, MacIntyre K, Simpson CR, et al. Long-Term Trends in First Hospitalization for Heart Failure and Subsequent Survival Between 1986 and 2003. *Circulation*. 2009;119:515-523.
11. Benjamin EJ, Virani SS, Callaway CW et al. Heart Disease and Stroke Statistics—2018 Update: A Report From the American Heart Association. *Circulation*. 2018;137:e67-e492.
12. Roger VL, Weston SA, Redfield MM, et al. Trends in Heart Failure Incidence and Survival in a Community-Based Population. *JAMA*. 2004;292:344-350.
13. Shannon M. Dunlay, Véronique L. Roger, Susan A. Weston, Ruoxiang Jiang, and Margaret M. Redfield (Circ Heart Fail. 2012;5:720-726.); Olmsted County community cohort of HF patients (1984 to 2009).

SIGNATURE

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

CYTOKINETICS, INCORPORATED

Date: May 23, 2022

By: /s/ Ching Jaw
Ching Jaw
Senior Vice President, Chief Financial Officer