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 17, 2021

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)

280 East Grand Avenue, 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.

On May 17, 2021 Cytokinetics, Incorporated (the "Registrant" or "Cytokinetics") announced that data from a secondary analysis of 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) assessing the effect of *omecamtiv mecarbil* on clinical outcomes in relationship to patient baseline ejection fraction were presented by John Teerlink, M.D., Professor of Medicine, University of California San Francisco, Director of Heart Failure, San Francisco Veterans Affairs Medical Center and Executive Committee Chair, GALACTIC-HF in a Late Breaking Clinical Trial session at the American College of Cardiology 70th Annual Scientific Session & Expo (ACC.21) and were simultaneously published in the *Journal of the American College of Cardiology*.[1]

In addition, on May 17, 2021, Cytokinetics announced that new findings from analyses of claims data and electronic health records related to heart failure ("HF") and hypertrophic cardiomyopathy ("HCM") were shared in two poster presentations at the American College of Cardiology 70th Annual Scientific Session & Expo (ACC.21). One poster presented data on spending for hospitalized Medicare patients with HF underscoring the economic burden of their healthcare, and an additional poster presented demographics and clinical characteristics of patients with hypertrophic cardiomyopathy.

GALACTIC-HF: Secondary Analysis

GALACTIC-HF enrolled 8,256 patients who were at risk of hospitalization and death, despite being well treated on standard of care therapy. As previously reported, after a median duration of follow-up of 21.8 months, the trial demonstrated a statistically significant effect of treatment with *omecamtiv mecarbil* to reduce risk of the primary composite endpoint of heart failure events (heart failure hospitalization and other urgent treatment for heart failure) or cardiovascular ("CV") death compared to placebo in patients treated with standard of care (hazard ratio, 0.92; 95% confidence interval [CI] 0.86, 0.99; p=0.025). No reduction in the secondary endpoint of time to CV death was observed in the overall population. [1] Supplemental analyses indicated that the effect of *omecamtiv mecarbil* on the primary composite endpoint was consistent across most prespecified subgroups, with a progressively larger treatment effect of *omecamtiv mecarbil* with decreasing EF (interaction p = 0.004). This secondary analysis further investigates the influence of EF on the observed treatment effects.

The analysis evaluated the effect of patient treatment with *omecamtiv mecarbil* based on quartiles of baseline EF defined as EF ≤22%, EF 23-28%, EF 29-32% and EF ≥33% as well as considering baseline EF as a continuous variable. The incidence of the primary outcome of first heart failure event or cardiovascular death increased with decreasing ejection fraction; in the lowest left ventricular ejection fraction ("LVEF") quartile (EF ≤22%) the incidence (35.6 per 100 patient-years) was almost 80% greater than in the highest EF quartile (EF ≥33%; 20 per 100 patient-years). Treatment with *omecamtiv mecarbil* demonstrated a 15% (HR 0.85; 95% CI 0.74-0.97; p = 0.016) and 17% (HR 0.83; 95% CI 0.73-0.95; p = 0.005) relative risk reduction in the lower two quartiles, respectively, compared to no difference in the upper two quartiles.

Analysis of ejection fraction as a continuous variable demonstrated a progressively larger treatment effect of *omecamtiv mecarbil* with decreasing ejection fraction (Figure A, interaction p = 0.013 by EF quartile). Accordingly, the absolute treatment effect on the primary composite endpoint also increased between the patients treated with placebo and *omecamtiv mecarbil* as baseline ejection fraction decreased (Figure B) such that in the lowest ejection fraction quartile, there was an absolute reduction of 7.4 events per 100 patient-years, with a number-needed-to-treat of 11.8 patients necessary to prevent an event over three years.

Figure A

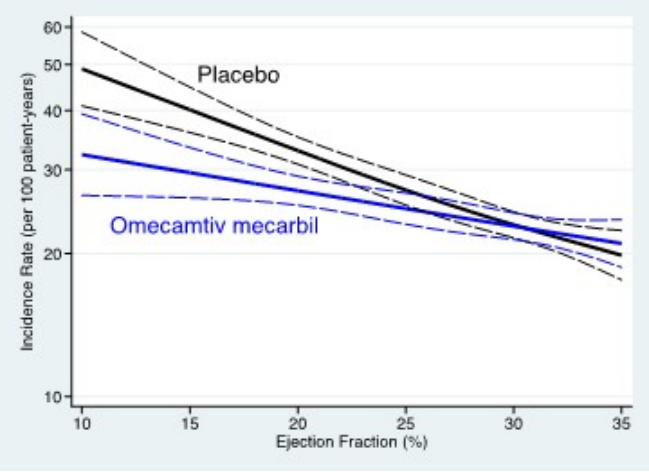
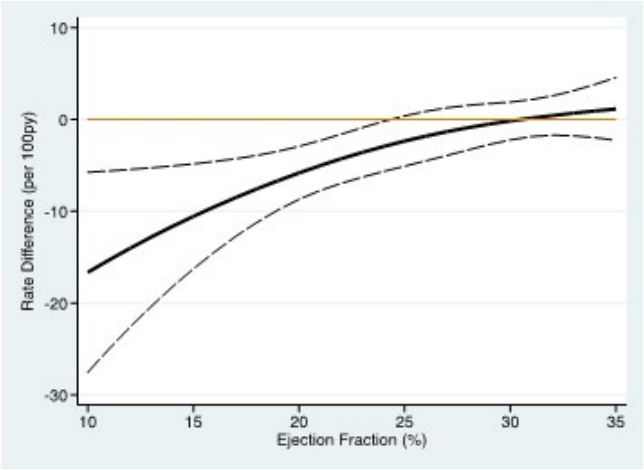


Figure B



The beneficial effect of treatment with *omecamtiv mecarbil* on the primary composite endpoint was driven predominantly by the reduction in heart failure events. To determine the significance of EF subgroup differences, a test of the interaction effect revealed that EF was a significant modifier of this treatment effect (interaction p = 0.004 by EF quartile, interaction p = 0.001 by EF as continuous variable). Treatment with *omecamtiv mecarbil* demonstrated a 19% (HR 0.81; 95% CI 0.70-0.93) and 17% (HR 0.84; 95% CI 0.72-0.98) relative risk reduction in the lower two quartiles, respectively, compared to no difference in the upper two quartiles.

A greater reduction in NT-proBNP was also observed with *omecamtiv mecarbil* in patients with lower EF, with a 22% reduction (p < 0.001) in the lowest EF quartile, and a 3% reduction in the highest quartile (p = 0.54; interaction p < 0.001). NT-proBNP is a biomarker of ventricular wall stress, where higher levels reflect more severe heart failure.

As previously noted, treatment with *omecamtiv mecarbil* resulted in a small reduction in heart rate (treatment difference of 1.1 to 1.9 bpm across the EF quartiles) and increase in troponin I (median 3-5 ng/L across the EF quartiles; limit of detection, 6 ng/L; upper reference limit, 40 ng/L), though these results did not differ by EF quartile. There were no significant differences in systolic blood pressure, serum potassium, or creatinine or the incidence of adverse events between the *omecamtiv mecarbil* and placebo treated groups between EF quartiles.

GALACTIC-HF: Trial Design and Primary Results

GALACTIC-HF,[2] one of the largest Phase 3 global cardiovascular outcomes studies in heart failure ever conducted, enrolled 8,256 patients in 35 countries across 945 sites with heart failure with reduced ejection fraction ("HFrEF"), New York Heart Association class II-IV, LVEF ≤35%, elevated natriuretic peptides and either current hospitalization for heart failure or history of hospitalization or emergency department visit for heart failure within a year. Patients were randomized to either oral placebo or a starting dose of 25 mg *omecamtiv mecarbil* twice daily (maintenance dose of 50 mg, 37.5 mg, or 25 mg twice daily) guided by pharmacokinetic-guided dose selection. A blood test, the QMS *Omecamtiv Mecarbil* Immunoassay (the OM Test) was used to measure plasma levels of *omecamtiv mecarbil* in each patient in order to guide selection of the appropriate maintenance dose.

The primary composite endpoint of this double-blind, placebo-controlled, event-driven trial was time to CV death or first heart failure event (heart failure hospitalization and other urgent treatment for heart failure). Secondary endpoints were: time to CV death, patient reported outcomes (measured by Kansas City Cardiomyopathy Questionnaire [KCCQ] Total Symptom Score [TSS]), time to first heart failure hospitalization and time to all-cause death. A first primary endpoint event occurred in 1,523 of 4,120 patients (37.0%) in the *omecamtiv mecarbil* group and in 1,607 of 4,112 patients (39.1%) in the placebo group (hazard ratio, 0.92; 95% confidence interval [CI] 0.86, 0.99; p=0.025). No reduction in the secondary endpoint of time to CV death was observed in the overall population. The effect on the primary endpoint was observed without evidence of an increase in the overall rates of myocardial ischemic events, ventricular arrhythmias or death from cardiovascular or all causes.

About *Omecamtiv Mecarbil* and the Phase 3 Clinical Trials Program

Omecamtiv mecarbil is an investigational selective cardiac myosin activator, the first of a novel class of myotropes[3] designed to directly target the contractile mechanisms of the heart, binding to and recruiting more cardiac myosin heads to interact with actin during systole. Preclinical research has shown that *omecamtiv mecarbil* increases cardiac contractility without increasing intracellular myocyte calcium concentrations or myocardial oxygen consumption.[4-6] 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.

Omecamtiv mecarbil is being developed for the potential treatment of HFrEF and is the subject of a comprehensive Phase 3 clinical trials program composed of GALACTIC-HF and METEORIC-HF (Multicenter Exercise Tolerance Evaluation of *Omecamtiv Mecarbil* Related to Increased Contractility in Heart Failure), a Phase 3 clinical trial designed to evaluate the effect of treatment with *omecamtiv mecarbil* compared to placebo on exercise capacity.

High Spending Among Medicare Patients Hospitalized with Heart Failure and Substantial Payments for Post-Acute Care

This analysis builds upon a previously presented analysis conducted in collaboration with Yale University School of Medicine examining payments spanning index hospitalization through 30-days post-discharge for Medicare beneficiaries with HF. Using Medicare fee-for-service administrative claims data, patients hospitalized with HF from 2016-2018 were identified with the following primary discharge diagnoses (ICD-10 codes): systolic HF (50.2 and 50.4), diastolic HF (50.3), hypertensive heart disease (HHD) with HF (I11), and HHD with HF and chronic kidney disease (I13). The total estimated mean Medicare 30-day payments for HF care were approximately $16.5 billion over the 3-year study period, with little change in spending year to year.

This new analysis of the same dataset examined 90-day post-discharge spending and found that the total estimated Medicare 90-day payments were approximately $27 billion over the 3-year study period. The index hospitalization accounted for 35% of the total mean 90-day payments. The remaining 65% of payments occurred in the post-acute care period (mean $11,374), driven by payments for readmission including observation stays (36% of post-acute care payments; mean $6,828) and skilled nursing facilities (27% of post-acute care payments; mean $5,192). Overall, 36% of Medicare patients hospitalized with HF were readmitted within 90 days. These results further emphasize the high cost of HF related health care, not only for initial hospitalization but for readmission and ongoing care.

Retrospective Observation of Patients with Obstructive HCM Finds Increase in Cardiovascular Comorbidities and Medication Use Over 2-Year Follow-Up

In a retrospective analysis of demographics and clinical characteristics of adult patients with obstructive HCM (“oHCM”), the first to examine a national sample using longitudinal medical and pharmacy claims data, patients were identified using claims data from the HealthCore Integrated Research Database (HIRD®), a database representing over 50 million people who are commercially insured or Medicare Advantage members in the United States, between January 1, 2012 to January 31, 2020. Patient characteristics and outcomes were reported for the 12-month period before the index date (the earliest diagnosis of oHCM) and a 2-year follow-up. Of the 1,841 patients identified with oHCM, 52% were male and the average age was 63.2 years. Cardiovascular comorbidities were common at the 2-year follow-up, including hypertension (64%), coronary artery disease (31%), atrial fibrillation (26%), HF (24%), and diabetes (21%). Between the 12-month baseline and 2-year follow up the percentage of patients with diagnostic procedures and myocardial imaging increased, as did the use of HCM-related medications ($p < 0.01$) including β-blockers (59% vs 70%), calcium channel blockers (29% vs 33%), anticoagulants (14% vs 22%), and antiarrhythmics (all: 6% vs 10%; disopyramide: 1% vs 3%). At the 2-year follow-up, 144 patients (8%) had received an implantable cardioverter-defibrillator for sudden death prevention and 123 patients (6%) underwent septal reduction procedures (5% myectomy; 1% alcohol septal ablation), with the mean time from initial evaluation to procedure being 218 days and 97 days, respectively. The results from this analysis, may help characterize the population of patients with oHCM and understand their disease progression to better support current treatment approaches and inform development of novel therapies to address this unmet need.

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 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 impact muscle function and contractility. Cytokinetics is engaging with regulatory authorities in preparation for a U.S. NDA submission of *omecamtiv mecarbil*, its novel cardiac muscle activator, following positive results from GALACTIC-HF, a large, international Phase 3 clinical trial in patients with heart failure. Cytokinetics is conducting METEORIC-HF, a second Phase 3 clinical trial of *omecamtiv mecarbil*. Cytokinetics is also developing CK-274, a next-generation cardiac myosin inhibitor, for the potential treatment of hypertrophic cardiomyopathies ("HCM"). Cytokinetics is conducting REDWOOD-HCM, a Phase 2 clinical trial of CK-274 in patients with obstructive HCM. Cytokinetics is also developing *reldesemtiv*, a fast skeletal muscle troponin activator for the potential treatment of ALS and other neuromuscular indications following conduct of FORTITUDE-ALS and other Phase 2 clinical trials. The company is preparing for the potential advancement of *reldesemtiv* to a Phase 3 clinical trial in 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, the potential benefits of *omecamtiv mecarbil*, including its ability to represent a novel therapeutic strategy to increase cardiac muscle function and restore cardiac performance; the timing and likelihood of any regulatory submissions or approval of *omecamtiv mecarbil*, Cytokinetics' research and development activities; the design, timing, results, significance and utility of preclinical and clinical results; and the properties and potential benefits of Cytokinetics' other 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 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. Teerlink JR., Diaz R., Felker GM., et al. Effect of Ejection Fraction on Clinical Outcomes in Patients treated with Omecamtiv Mecarbil in GALACTIC-HF. *JACC*. 2021
2. Teerlink JR., Diaz R., Felker GM., et al. Omecamtiv Mecarbil in Chronic Heart Failure With Reduced Ejection Fraction: Rationale and Design of GALACTIC-HF. *JACC Heart Fail*. 2020 Apr; 8(4):329-340. doi: 10.1016/j.jchf.2019.12.001.Epub 2020 Feb 6.
3. Psotka MA, Gottlieb SS, Francis GS et al. Cardiac Calcitropes, Myotropes, and Mitotropes. *JACC*. 2019; 73:2345-53.
4. 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.
5. 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.
6. 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.
7. James et al. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. *Lancet* 2018; 392: 1789-858.
8. 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.
9. 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.
10. Roger VL. Epidemiology of Heart Failure. *Circulation Research*. 2013;113:646-659, originally published August 29, 2013. Doi: 10.1161/CIRCRESAHA.113.300268.
11. 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.
12. 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.
13. 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.
14. 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.
15. 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 Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

CYTOKINETICS, INCORPORATED

Date: May 17, 2021

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