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): June 30, 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 June 30, 2021 Cytokinetics, Incorporated (the "Registrant" or "Cytokinetics") announced that additional results 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) were presented at Heart Failure 2021, an International Congress of the European Society of Cardiology, including a prespecified subgroup analysis of the influence of atrial fibrillation or flutter ("AFF") on the treatment effect of *omecamtiv mecarbil* in a Late Breaking Clinical Trial Session. Other analyses were presented in the Clinical Trial Updates Session related to which patients in GALACTIC-HF achieved an increased treatment effect with *omecamtiv mecarbil.*

GALACTIC-HF: Patients Without Atrial Fibrillation or Flutter Have Increased Treatment Effect with *Omecamtiv Mecarbil*

Scott Solomon, M.D., the Edward D. Frohlich Distinguished Chair, Professor of Medicine, Harvard Medical School and Director of Noninvasive Cardiology, Brigham and Women's Hospital, presented additional analyses from GALACTIC-HF assessing how baseline AFF in patients impacted the effectiveness of *omecamtiv mecarbil* in GALACTIC-HF. Of the 8,256 patients enrolled in GALACTIC-HF, 2,245 patients (27%) had AFF at baseline; these patients were older, more likely to be randomized as inpatients, had a higher New York Heart Association ("NYHA") class and had higher NT-proBNP compared to patients without AFF. The effect of treatment with *omecamtiv mecarbil* on the primary composite endpoint of heart failure events (heart failure hospitalization and other urgent treatment for heart failure) or cardiovascular ("CV") death was greater in patients without baseline AFF compared to those patients with AFF at baseline (interaction p=0.012). Importantly, the modification of the treatment effect by AFF was concentrated in patients with AFF using digoxin (n=692) with minimal evidence of effect modification in patients with AFF not using digoxin (n=1553). Digoxin did not modify the treatment effect of *omecamtiv mecarbil* in patients without AFF. These findings suggest caution should be exercised when treating patients with AFF using both digoxin and *omecamtiv mecarbil.* Interestingly, given prior observations of the positive impact of *omecamtiv mecarbil* on left atrial function, an exploratory analysis from GALACTIC-HF indicated fewer serious adverse events of atrial fibrillation in patients without AFF at baseline in patients treated with *omecamtiv mecarbil* compared to placebo (55 events in 2,974 patients treated with *omecamtiv mecarbil* vs. 78 events in 3,013 patients treated with placebo, p=0.046).

GALACTIC-HF: Patients with Higher Baseline NT-proBNP Have Increased Treatment Effect with *Omecamtiv Mecarbil*

In a separate analysis, John McMurray, M.D., Professor of Medical Cardiology & Honorary Consultant Cardiologist, Institute of Cardiovascular & Medical Sciences, BHF Cardiovascular Research Centre, University of Glasgow, presented analyses on the effect of treatment with *omecamtiv mecarbil* according to baseline NT-proBNP in patients without AFF, as well as in all patients in GALACTIC-HF. NT-proBNP is a biomarker of ventricular wall stress in which higher levels reflect more severe heart failure. Among the 5,971 patients who did not have AFF, the median (Q1, Q3) NT-proBNP level was 1,675 (812-3579 pg/ml). In patients without AFF, the treatment effect of *omecamtiv mecarbil* on the primary composite endpoint was increased in patients with a baseline NT-proBNP above the median (hazard ratio, 0.81; 95% confidence interval 0.73-0.90) compared to patients with baseline NT-proBNP equal to or below the median (HR, 0.94; 95% CI 0.80-1.09; interaction p=0.095). The same pattern was observed in the overall population in which patients with a baseline NT-proBNP greater than the median experienced an increased treatment effect (HR, 0.88; 95% CI 0.80-0.96) compared to patients with a baseline NT-proBNP equal to or below the median (HR, 1.01; 95% CI 0.90-1.15; interaction p=0.035.) Examined as a continuous variable, there was an interaction between treatment with *omecamtiv mecarbil* and baseline NT-proBNP that showed an increased treatment effect on the primary outcome in patients as baseline NT-proBNP increased both in those without AFF (interaction p=0.024) and in the overall population (interaction p=0.005). These findings suggest the benefit of treatment with *omecamtiv mecarbil* increased progressively as baseline NT-proBNP increased consistent with other analyses from GALACTIC-HF that suggest more severe heart failure patients may derive increased benefit from treatment with *omecamtiv mecarbil*.

GALACTIC-HF: Patients with Severe Heart Failure Have Increased Treatment Effect with *Omecamtiv Mecarbil*

Michael Felker, M.D., Professor of Medicine, Duke Clinical Research Institute presented an analysis of the treatment effect of *omecamtiv mecarbil* on the primary composite endpoint in patients from GALACTIC-HF classified as having severe heart failure based on modified criteria from the Heart Failure Association of the European Society of Cardiology (ESC-HFA) advanced heart failure position statement. Patients in this subgroup had NYHA class III-IV symptoms, EF ≤ 30%, and hospitalization for heart failure within the prior six months. Of patients enrolled in GALACTIC-HF, 2,258 (27%) met these criteria for severe heart failure. Patients with severe heart failure had markers of more advanced disease and higher baseline risk, with event rates in patients treated with placebo that were approximately twice those of patients without severe heart failure. In patients with severe heart failure, the treatment effect of *omecamtiv mecarbil* on the primary composite endpoint was increased (HR, 0.80; 95% CI 0.71-0.90) compared to patients without severe heart failure (HR, 0.99; 95% CI 0.91-1.08; interaction p=0.005). The results for CV death were qualitatively similar; patients with severe heart failure experienced a trend towards treatment benefit from *omecamtiv mecarbil* (HR, 0.88; 95% CI 0.75-1.03) while patients without severe heart failure did not (HR, 1.10, 95% CI 0.97-1.25; interaction p=0.028). Furthermore, as the severity of heart failure increased, as indicated by the number of the three severity criteria met, both the incidence of the primary composite endpoint and the treatment effect of *omecamtiv mecarbil* increased. *Omecamtiv mecarbil* was equally well tolerated in patients with and without severe heart failure, with no significant changes in blood pressure, renal function, or potassium compared to placebo. These results from GALACTIC-HF demonstrate a potentially clinically important treatment effect of *omecamtiv mecarbil* in patients with severe heart failure.

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[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. Preclinical research has shown that *omecamtiv mecarbil* increases cardiac contractility without increasing intracellular myocyte calcium concentrations or myocardial oxygen consumption.[2-4] 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. The results from GALACTIC-HF, published in the *New England Journal of Medicine*, demonstrated a statistically significant effect of treatment with *omecamtiv mecarbil* to reduce risk of the primary composite endpoint of time to first heart failure event (heart failure hospitalization and other urgent treatment for heart failure) or 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.[5] Supplemental analyses indicated a greater treatment effect in patients with a lower LVEF (LVEF ≤28%, n=4,456, hazard ratio, 0.84; 95% CI 0.77, 0.92; interaction p=0.003). Effects in GALACTIC-HF were observed without evidence of an increase in the overall rates of myocardial ischemic events, ventricular arrhythmias or death from cardiovascular or all causes.

About Heart Failure

Heart failure is a grievous condition that affects more than 64 million people worldwide[6] about half of whom have reduced left ventricular function.[7,8] It is the leading cause of hospitalization and readmission in people age 65 and older.[9,10] Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor.[11] 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 are expected to die within five years of initial hospitalization.[12,13] More than 2 million people in the U.S. are estimated to have an ejection fraction <30%, indicating they may have severe heart failure.[14]

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 preparing a U.S. NDA submission of *omecamtiv mecarbil*, its novel cardiac muscle activator, based on positive results from GALACTIC-HF, a large, international Phase 3 clinical trial in patients with heart failure. Cytokinetics is also 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 CK-274 to a Phase 3 clinical trial in obstructive HCM and *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*, the potential number of patients that could benefit from treatment with *omecamtiv mecarbil*, the potential advancement of *reldesemtiv* to a phase 3 clinical trial in ALS, Cytokinetics' other 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.

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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: June 30, 2021

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