Cytokinetics Presents New Data Relating to Aficamten and Hypertrophic Cardiomyopathy at the American Heart Association Scientific Sessions 2024

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Two New Analyses from SEQUOIA-HCM Demonstrate Treatment with Aficamten Improves Post-Exercise Oxygen Uptake Recovery and Quality of Life

New Data from FOREST-HCM Demonstrate Aficamten Durably Reduces the Proportion of Patients Guideline Eligible for Septal Reduction Therapy

Analyses of Real-World Data Reveal Cost of Care Differences in HCM Across Gender, Age and Race/Ethnicity

SOUTH SAN FRANCISCO, Calif., Nov. 16, 2024 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced new data relating to *aficamten* and hypertrophic cardiomyopathy (HCM), were presented at the American Heart Association Scientific Sessions 2024 in Chicago, IL.

"These analyses add to the growing body of evidence supporting the safety and efficacy profile of *aficamten* and build upon primary findings related to peak VO_2 and improvement in health-related quality of life, while demonstrating a significant and durable reduction in the need for septal reduction therapy," said Stephen Heitner, M.D., Vice President, Head of Clinical Research. "In addition, analyses presented of real-world data shed light on the disparities that exist in the cost of care for HCM, underscoring the need for improved equity in healthcare across gender and race."

Treatment with *Aficamten* Improves VO_2 Recovery

Data from a pre-specified exploratory analysis from SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***A**ficamten* in **HCM**) presented today showed that treatment with *aficamten* from baseline to Week 24 resulted in significantly shortened post-exercise oxygen-uptake (VO_2) recovery (VO_2Rec). Prolonged VO_2Rec has previously been linked to adverse outcomes in patients with other forms of heart failure. The analysis demonstrated that treatment with *aficamten* significantly shortened times for VO_2Rec to decline by 12.5% (VO_2Rec $T_{12.5\%}$), 25% (VO_2Rec $T_{25\%}$) and 50% (VO_2Rec $T_{50\%}$) of peak VO_2, corresponding to absolute reductions relative to placebo of 8 seconds (p<0.001), 7 seconds (p<0.001) and 8 seconds (p=0.01), respectively (Table 1). Additionally, a decrease in VO_2Rec $T_{12.5\%}$ corresponded to a decrease in NT-proBNP levels (p<0.001), high-sensitivity cardiac troponin I levels (hs-cTnI) (p<0.001), resting left ventricular outflow tract gradient (LVOT-G) (p=0.003) and Valsalva LVOT-G (p=0.003).

Table 1. Effect of *Aficamten* on Post-Exercise Oxygen Uptake Recovery in Patients with Obstructive HCM

	AFICAMTEN				**PLACEBO**					
Variable	**n**	**Baseline**	**Week 24**	**Absolute difference (SD)**	**n**	**Baseline**	**Week 24**	**Absolute difference (SD)**	**Treatment Effect (95% CI)**	**p-value**
PeakVO_2 (mL/kg/min)	133	18.4 ± 4.5	20.2 ± 5.2	1.8 ± 3.1	130	18.6 ± 4.6	18.6 ± 4.7	0.0 ± 2.7	1.7 (1.0, 2.4)	p<0.001
VO_2Rec Delay 0% (s)	134	19 ± 20	15 ± 18	-4 ± 19	129	17 ± 19	18 ± 19	1 ± 19	-4 (-8, -0)	p=0.047
VO_2recovery 12.5% (s)	126	45 ± 20	38 ± 18	-7 ± 19	127	45 ± 22	46 ± 23	1 ± 16	-8 (-12, -5)	p<0.001
VO_2recovery 25% (s)	123	66 ± 21	60 ± 19	-6 ± 18	126	70 ± 27	70 ± 28	-0 ± 17	-7 (-11, -3)	p<0.001
VO_2recovery 50% (s)	117	115 ± 32	107 ± 32	-8 ± 27	116	116 ± 38	116 ± 36	0 ± 26	-8 (-15, -2)	p=0.01

Treatment with *Aficamten* Results in Sustained and Significant Improvements in Health-Related Quality of Life

Data were also presented from an additional pre-specified exploratory analysis of SEQUOIA-HCM that evaluated the effect of *aficamten* on patient-reported health status using two quality of life (QoL) measurements, EuroQol 5-Dimension 5-Level (EQ-5D-5L) and EuroQol Visual Analogue Scale (EQ-VAS). EQ-5D-5L (range from 0 to 1) and EQ-VAS (range from 0 to 100) were measured at baseline through Week 24, with higher scores indicating better QoL. At baseline, there were no differences between patients receiving *aficamten* and placebo in any of the five domains of the EQ-5D-5L index. Treatment with *aficamten* improved the EQ-5D-5L index score by 0.04 (p=0.008) and the EQ-VAS score by 4.5 points (p=0.002) compared to placebo, with significant differences observed as early as eight weeks after treatment initiation (p=0.005). Following withdrawal of treatment at the end of the clinical trial, QoL benefits in patients who were receiving *aficamten* subsequently decreased. These data demonstrate that treatment with *aficamten* yielded early, sustained and significant improvement in overall health-related QoL among patients with obstructive HCM as measured by EQ-5D-5L, reinforcing previously reported data showing that *aficamten* improves QoL as measured by Kansas City Cardiomyopathy Questionnaire (KCCQ).

Treatment with *Aficamten* Durably Reduces SRT-Eligibility After 12 Weeks in Open-Label Extension

Findings from an analysis from FOREST-HCM (**F**ollow-Up, **O**pen-Label, **R**esearch **E**valuation of **S**ustained **T**reatment with *Aficamten* in **HCM**), the open-label extension clinical study of *aficamten* in patients with HCM, related to the efficacy and safety of *aficamten* in patients who at baseline were guideline-eligible for septal reduction therapy (SRT) were also presented. Of the 280 patients with obstructive HCM enrolled in FOREST-HCM with ≥12 weeks of follow-up at the time of this analysis, 97 (35%) met guideline eligibility criteria for SRT at baseline; after 12 weeks of treatment with *aficamten*, only 3 (3%) remained SRT guideline-eligible. When comparing those patients who were SRT guideline-eligible versus those who were not at baseline, there were similar, robust improvements in KCCQ, New York Heart Association (NYHA) Functional Class, NT-proBNP and resting and Valsalva left ventricular outflow tract (LVOT) gradient. Changes in left ventricular ejection fraction (LVEF) were modest and similar between SRT-eligible and SRT-ineligible patients. Instances of LVEF <50% and atrial fibrillation or flutter were rare, and similar between groups. These results demonstrate that treatment with *aficamten* may provide a safe, durable and effective alternative to SRT in many patients with obstructive HCM.

Analyses of Real-World Data Reveals Differences in Costs Across Gender, Age and Race/Ethnicity in Patients with Obstructive HCM

A new health economics and outcomes research (HEOR) study presented today evaluated the impact of sociodemographic characteristics on cost of care in patients with obstructive HCM. These retrospective analyses included adults diagnosed with obstructive HCM from January 2013 to December 2021 using real-world data from Optum Market Clarity database. Among 5,129 patients identified with obstructive HCM, 52% were female, the mean age was 63.9 years, 77.6% were white and 40% were Medicare recipients. Compared to females, male patients had higher costs including overall total ($71,581 vs $63,710; p=0.014), medical ($70,395 vs $62,455; p=0.013), ambulatory ($16,024 vs $10,776; p<0.001), office visits ($1,906 vs $1,573; p<0.001) and outpatient visits ($14,118 vs $9,202; p<0.001). Compared to white patients, Black patients had significantly higher inpatient admissions costs ($54,572 vs $42,686; p=0.015), Hispanic patients had greater emergency room costs ($1,724 vs $791; p<0.001) and Asian patients had greater office costs ($2,094 vs $1,800; p<0.001). Patients aged 18-39 years had higher costs across all categories (p<0.001) compared to patients 40 or older, except inpatient admissions and prescriptions. Overall, these real-world analyses showed that, for patients with obstructive HCM, being a younger male was associated with increased healthcare costs, with additional differences in cost across race/ethnicity.

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 potential long-term effects on cardiac structure and function. *Aficamten* was evaluated in SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***A**ficamten* in **HCM**), a positive pivotal Phase 3 clinical trial in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). *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. Cytokinetics submitted a New Drug Application (NDA) to the FDA in Q3 2024 and expects to submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) in Q4 2024.

Aficamten is also currently being evaluated in MAPLE-HCM, a Phase 3 clinical trial of *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM, ACACIA-HCM, a Phase 3 clinical trial of *aficamten* in patients with non-obstructive HCM, and CEDAR-HCM, a clinical trial of *aficamten* in a pediatric population with obstructive HCM, and FOREST-HCM, an open-label extension clinical study of *aficamten* in patients with HCM.

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 reduced exercise capacity and symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity. HCM is the most common monogenic inherited cardiovascular disorder, with approximately 280,000 patients diagnosed, however, there are an estimated 400,000-800,000 additional patients who remain undiagnosed in the U.S.[1,2,3] Two-thirds of patients with HCM have obstructive HCM (oHCM), where the thickening of the cardiac muscle leads to left ventricular outflow tract (LVOT) obstruction, while one-third have non-obstructive HCM (nHCM), where blood flow isn't impacted, but the heart muscle is still thickened. People with HCM are at high risk of also developing cardiovascular complications including atrial fibrillation, stroke and mitral valve disease.[4] People with HCM are at risk for potentially fatal ventricular arrhythmias and it is one of the leading causes of sudden cardiac death in younger people or athletes.[5] A subset of patients with HCM are at high risk of progressive disease leading to dilated cardiomyopathy and heart failure necessitating cardiac transplantation.

About Cytokinetics

Cytokinetics is a late-stage, specialty cardiovascular biopharmaceutical company focused on discovering, developing and commercializing muscle biology-directed drug candidates as potential treatments for debilitating diseases in which cardiac 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 myocardial muscle function and contractility. Following positive results from SEQUOIA-HCM, the pivotal Phase 3 clinical trial evaluating *aficamten,* a next-in-class cardiac myosin inhibitor, in obstructive hypertrophic cardiomyopathy (HCM), Cytokinetics submitted an NDA for *aficamten* to the U.S. Food & Drug Administration and is progressing regulatory submissions for *aficamten* for the treatment of obstructive HCM in Europe. *Aficamten* is also currently being evaluated in MAPLE-HCM, a Phase 3 clinical trial of *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM, ACACIA-HCM, a Phase 3 clinical trial of *aficamten* in patients with non-obstructive HCM, CEDAR-HCM, a clinical trial of *aficamten* in a pediatric population with obstructive HCM, and FOREST-HCM, an open-label extension clinical study of *aficamten* in patients with HCM. Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac muscle activator, in patients with heart failure with severely reduced ejection fraction (HFrEF), CK-586, a cardiac myosin inhibitor with a mechanism of action distinct from *aficamten* for the potential treatment of heart failure with preserved ejection fraction (HFpEF), and CK-089, a fast skeletal muscle troponin activator (FSTA) for the potential treatment of a specific type of muscular dystrophy.

For additional information about Cytokinetics, visit www.cytokinetics.com and follow us on X, LinkedIn, Facebook and YouTube.

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 express or implied relating to the properties or potential benefits of *aficamten* or any of our other drug candidates, our ability to obtain regulatory approval for *aficamten* for the treatment of obstructive hypertrophic cardiomyopathy or any other indication from FDA or any other regulatory body in the United States or abroad, and the labeling or post-marketing conditions that FDA or another regulatory body may require in connection with the approval of *aficamten.* 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 the risks related to Cytokinetics' business outlines in Cytokinetics' filings with the Securities and Exchange Commission. Forward-looking statements are not guarantees of future performance, and Cytokinetics' actual results of operations, financial condition and liquidity, and the development of the industry in which it operates, may differ materially from the forward-looking statements contained in this press release. Any forward-looking statements that Cytokinetics makes in this press release speak only as of the date of this press release. Cytokinetics assumes no obligation to update its forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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