Cytokinetics Announces Start of CEDAR-HCM, a Clinical Trial of Aficamten in a Pediatric Population With Symptomatic Obstructive Hypertrophic Cardiomyopathy

May 8, 2024 11:30 AM EDT

SOUTH SAN FRANCISCO, Calif., May 08, 2024 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that CEDAR-HCM (**C**linical **E**valuation of **D**osing with ***A**ficamten* to **R**educe Obstruction in a Pediatric Population in **HCM**), a clinical trial of *aficamten* in a pediatric population with symptomatic obstructive hypertrophic cardiomyopathy (HCM), is open to enrollment. *Aficamten* is a next-in-class cardiac myosin inhibitor in development for the potential treatment of HCM.

"We are pleased to further expand the broad development program for *aficamten* with the start of CEDAR-HCM, a trial assessing the safety and efficacy of a cardiac myosin inhibitor in a pediatric population," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "As a genetic disease, HCM often casts a shadow over entire families, including adolescents and children where it is associated with a high risk of heart failure and serious arrhythmias. HCM can present similarly in adolescents and children as it does in adults and may negatively impact overall quality of life. By evaluating the efficacy and safety of *aficamten* in another very important group of people, our aim is to provide all members of families impacted by HCM with a potential new treatment option."

CEDAR-HCM: Clinical Trial Design

CEDAR-HCM is a multi-center, randomized, double-blind, placebo-controlled and open-label extension clinical trial to evaluate the efficacy, pharmacokinetics (PK) and safety of *aficamten* in a pediatric population with symptomatic obstructive HCM. The primary endpoint is the change in Valsalva left ventricular outflow tract gradient (LVOT-G) from baseline to Week 12. Secondary endpoints include the change from baseline to Week 12 in resting LVOT-G, New York Heart Association (NYHA) Functional Class, pharmacokinetics and cardiac biomarkers including NT-proBNP and hs-cTnI.

CEDAR-HCM is expected to enroll two cohorts, beginning with an initial cohort of approximately 40 adolescent patients aged 12 to 17. Adolescent patients enrolled in CEDAR-HCM must have LVEF ≥ 60%, Valsalva LVOT-G ≥ 50 mmHg and NYHA Functional Class ≥ II. Patients will be randomized on a 2:1 basis to receive *aficamten* or placebo, and those receiving *aficamten* will begin with 5 mg dosed once daily. At weeks 2, 4 and 6 patients will receive an echocardiogram to determine if they will be up-titrated to escalating doses of 10, 15 or 20 mg. Dose escalation will occur only if a patient has a Valsalva LVOT-G ≥ 30 mmHg and an LVEF ≥ 55%. Safety, efficacy and PK data obtained from at least 20 adolescent patients who have completed 12 weeks of double-blind treatment will support the decision to open enrollment in a second cohort of approximately 8 to 10 younger patients (aged 6 to 11). The protocol will be amended to include eligibility criteria and dose selection for the younger pediatric cohort. After 12 weeks of double-blind treatment, eligible patients will rollover into the open label extension period of CEDAR-HCM. Additional information can be found on www.clinicaltrials.gov.

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.

About the Broad Phase 3 Clinical Trials Program for *Aficamten*

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.

SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***A**ficamten* in **HCM**), was the pivotal Phase 3 clinical trial in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). The results from SEQUOIA-HCM show that treatment with *aficamten* significantly improved exercise capacity compared to placebo, increasing peak oxygen uptake (pVO_2) measured by cardiopulmonary exercise testing (CPET) by a least square mean difference (95% CI) of 1.74 (1.04 - 2.44) mL/kg/min (p=0.000002). The treatment effect with *aficamten* was consistent across all prespecified subgroups reflective of patient baseline characteristics and treatment strategies, including patients receiving or not receiving background beta-blocker therapy. Statistically significant (p<0.0001) and clinically meaningful improvements were also observed in all 10 prespecified secondary endpoints. *Aficamten* was well-tolerated with an adverse event profile comparable to placebo. Treatment emergent serious adverse events occurred in 8 (5.6%) and 13 (9.3%) patients on *aficamten* and placebo, respectively. Core echocardiographic left ventricular ejection fraction (LVEF) was observed to be <50% in 5 patients (3.5%) on *aficamten* compared to 1 patient (0.7%) on placebo. There were no instances of worsening heart failure or treatment interruptions due to low LVEF.

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 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.

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 in the U.S., however, there are an estimated 400,000-800,000 additional patients who remain undiagnosed.[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 first-in-class muscle activators and next-in-class muscle inhibitors 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. Cytokinetics is preparing for regulatory submissions for *aficamten*, its next-in-class cardiac myosin inhibitor, following positive results from SEQUOIA-HCM, the pivotal Phase 3 clinical trial in obstructive hypertrophic cardiomyopathy. *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 hypertrophic cardiomyopathy (HCM). Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac muscle activator, in patients with heart failure. Additionally, Cytokinetics is developing CK-586, a cardiac myosin inhibitor with a mechanism of action distinct from *aficamten* for the potential treatment of HFpEF, and CK-136, a cardiac troponin activator for the potential treatment HFrEF and other types of heart failure, such as right ventricular failure resulting from impaired cardiac contractility.

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 and our ability to fully enroll CEDAR-HCM. 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.

Contact:
Cytokinetics
Diane Weiser
Senior Vice President, Corporate Affairs
(415) 290-7757

References:

1. CVrg: Heart Failure 2020-2029, p 44; Maron et al. 2013 DOI: 10.1016/S0140-6736(12)60397-3; Maron et al 2018 10.1056/NEJMra1710575
2. Symphony Health 2016-2021 Patient Claims Data DoF;
3. Maron MS, Hellawell JL, Lucove JC, Farzaneh-Far R, Olivotto I. Occurrence of Clinically Diagnosed Hypertrophic Cardiomyopathy in the United States. Am J Cardiol. 2016; 15;117(10):1651-1654.
4. Gersh, B.J., Maron, B.J., Bonow, R.O., Dearani, J.A., Fifer, M.A., Link, M.S., et al. 2011 ACCF/AHA guidelines for the diagnosis and treatment of hypertrophic cardiomyopathy. A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Journal of the American College of Cardiology and Circulation, 58, e212-260.
5. Hong Y, Su WW, Li X. Risk factors of sudden cardiac death in hypertrophic cardiomyopathy. Current Opinion in Cardiology. 2022 Jan 1;37(1):15-21

Source: Cytokinetics, Incorporated