



Amgen, Cytokinetics and Servier Announce Topline Results From GALACTIC-HF, a Phase 3 Trial of Omecamtiv Mecarbil in Patients With Heart Failure

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**Trial Met Primary Composite Endpoint
of Reduction in Cardiovascular Death or Heart Failure Events**

**Trial Did Not Meet Secondary Endpoint
of Reduction in Cardiovascular Death**

**Results Will Be Presented in Late Breaking Clinical Trial Session
at AHA Scientific Sessions 2020**

THOUSAND OAKS, Calif. and SOUTH SAN FRANCISCO, Calif. and SURESNES, France, Oct. 08, 2020 (GLOBE NEWSWIRE) -- Amgen (NASDAQ:AMGN), Cytokinetics, Incorporated (NASDAQ:CYTK) and Servier today announced topline results from GALACTIC-HF, a Phase 3 pivotal clinical trial of omecamtiv mecarbil in patients with heart failure with reduced ejection fraction (HFrEF).

The results of GALACTIC-HF show that treatment with omecamtiv mecarbil achieved the primary composite efficacy endpoint and demonstrated a statistically significant effect to reduce 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 (HR: 0.92; 95% CI: 0.86, 0.99, p=0.0252).

No reduction in the secondary endpoint of CV death was observed. Adverse events, including major ischemic cardiac events, were balanced between treatment arms. Additional analyses of data are underway and results from GALACTIC-HF will be presented at the American Heart Association (AHA) Scientific Sessions 2020, in a virtual Late Breaking Clinical Trial session on Friday, November 13, 2020 from 10:35-10.45 a.m. CDT.

Omecamtiv mecarbil is an investigational cardiac myosin activator, the first of a novel class of myotropes¹ designed to directly target the contractile mechanisms of the heart.

"The outcomes observed in GALACTIC-HF further the understanding of treating heart failure, a devastating disease in which half of heart failure patients will die within five years of initial hospitalization," said David M. Reese, M.D. executive vice president of Research and Development at Amgen. "At Amgen, we remain committed to developing and delivering transformative medicines that improve the lives of patients with cardiovascular disease."

"GALACTIC-HF provides insights into effects associated with targeting cardiac muscle contractility with omecamtiv mecarbil to treat heart failure patients with reduced ejection fraction," said Fady I. Malik, M.D., Ph.D., Cytokinetics' executive vice president of Research & Development. "We are grateful to the trial investigators, site personnel, patients and caregivers who participated in the trial, and we look forward to further data analyses and the presentation of the results of this Phase 3 trial at the American Heart Association Scientific Sessions."

"Heart failure is a devastating condition jeopardizing patients' lives every day. We are pleased to have collaborated with Amgen and Cytokinetics on one of the largest heart failure trials ever conducted to investigate this novel therapy in patients with heart failure. It is important to now turn our attention to fully analyzing the data from this important study in this clinical setting," said Claude Bertrand, PharmD, PhD, Executive Vice President R&D at Servier.

GALACTIC-HF: Trial Design

GALACTIC-HF,² (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure), one of the largest Phase 3 global cardiovascular outcomes studies in heart failure ever conducted, enrolled 8,256 patients in 35 countries with HFrEF, New York Heart Association (NYHA) class II-IV, left ventricular ejection fraction (LVEF) \leq 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.

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 myotropes¹ 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.³⁻⁵ 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 heart failure with reduced ejection fraction (HFrEF) under a collaboration between Amgen and Cytokinetics, with funding and strategic support from Servier. Omecamtiv mecarbil 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.

About Heart Failure

Heart failure is a grievous condition that affects more than 64 million people worldwide⁶ 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 will die within five years of initial hospitalization.^{12,13}

About Cytokinetics and Amgen Collaboration

In 2006, Cytokinetics and Amgen entered into a strategic alliance to discover, develop and commercialize novel small molecule therapeutics designed to activate the cardiac sarcomere for the potential treatment of heart failure. Omecamtiv mecarbil is being developed by Amgen in collaboration with Cytokinetics, with funding and strategic support from Servier. Amgen holds an exclusive, worldwide license to omecamtiv mecarbil and related compounds, subject to Cytokinetics' specified development and commercialization rights. Cytokinetics is eligible for pre-commercialization and commercialization milestone payments and royalties that escalate based on increasing levels of annual net sales of products commercialized under the agreement. Cytokinetics has co-invested with Amgen in the Phase 3 development program of omecamtiv mecarbil in exchange for increased royalties from Amgen on worldwide sales of omecamtiv mecarbil outside Japan and co-promotion rights in institutional care settings in North America. Amgen has also entered an alliance with Servier for exclusive commercialization rights for omecamtiv mecarbil in Europe as well as the Commonwealth of Independent States, including Russia. Servier contributes funding for development and provides strategic support to the program.

About Amgen

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its biologics manufacturing expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be the world's largest independent biotechnology company, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

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 collaborating with Amgen Inc. (Amgen) to develop omecamtiv mecarbil, a novel cardiac muscle activator. Omecamtiv mecarbil is the subject of an international clinical trials program in patients with heart failure including GALACTIC-HF and METEORIC-HF. Amgen holds an exclusive worldwide license to develop and commercialize omecamtiv mecarbil with a sublicense held by Servier for commercialization in Europe and certain other countries. Cytokinetics is developing *reldesemtiv*, a fast skeletal muscle troponin activator (FSTA) for the potential treatment of ALS and other neuromuscular indications following conduct of FORTITUDE-ALS and other Phase 2 clinical trials. The company is considering potential advancement of *reldesemtiv* to Phase 3 pending ongoing regulatory interactions. Cytokinetics is collaborating with Astellas Pharma Inc. (Astellas) to research, develop and commercialize other novel mechanism skeletal sarcomere activators (not including FSTAs). Licenses held by Amgen and Astellas are subject to specified co-development and co-commercialization rights of Cytokinetics. Cytokinetics is also developing CK-274, a novel cardiac myosin inhibitor that company scientists discovered independent of its collaborations, for the potential treatment of hypertrophic cardiomyopathies. Cytokinetics has granted Ji Xing Pharmaceuticals Limited an exclusive license to develop and commercialize CK-274 in China and Taiwan, in accordance with Cytokinetics' planned global registration programs. Cytokinetics is conducting REDWOOD-HCM, a Phase 2 clinical trial of CK-274 in patients with obstructive HCM. 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.

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

About Servier

Servier is an international pharmaceutical company governed by a non-profit foundation, with its headquarters in France (Suresnes). With a strong international presence in 150 countries and a turnover of 4.6 billion euros in 2019, Servier employs 22,000 people worldwide. Entirely independent, the Group reinvests in average 25% of its turnover (excluding generics) every year in research and development and uses all its profits for development. Corporate growth is driven by Servier's constant commitment in five areas of excellence: cardiovascular, immune-inflammatory and neurodegenerative diseases, cancer and diabetes, as well as by its activities in high-quality generic drugs. Servier also offers eHealth solutions beyond drug development.

More information: www.servier.com

Amgen Forward-Looking Statements

This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including any statements on the outcome, benefits and synergies of collaborations, or potential collaborations, with any other company, including BeiGene, Ltd. or any collaboration or potential collaboration in pursuit of therapeutic antibodies against COVID-19 (including statements regarding such collaboration's, or our own, ability to discover and develop fully-human neutralizing antibodies targeting SARS-CoV-2 or antibodies against targets other than the SARS-CoV-2 receptor binding domain, and/or to produce any such antibodies to potentially prevent or treat COVID-19), or the Otezla[®] (apremilast) acquisition, including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion, as well as estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes, effects of pandemics or other widespread health problems such as the ongoing COVID-19 pandemic on our business, outcomes, progress, or effects relating to studies of Otezla as a potential treatment for COVID-19, and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission reports filed by Amgen, including its most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

No forward-looking statement can be guaranteed and actual results may differ materially from those Amgen projects. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for Amgen to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expects similar variability in the future. Even when clinical trials are successful, regulatory authorities may question the

sufficiency for approval of the trial endpoints Amgen has selected. Amgen develops product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as Amgen may have believed at the time of entering into such relationship. Also, Amgen or others could identify safety, side effects or manufacturing problems with its products, including its devices, after they are on the market.

Amgen's results may be affected by its ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing its products and global economic conditions. In addition, sales of Amgen's products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, Amgen's research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Amgen's business may be impacted by government investigations, litigation and product liability claims. In addition, Amgen's business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If Amgen fails to meet the compliance obligations in the corporate integrity agreement between Amgen and the U.S. government, Amgen could become subject to significant sanctions. Further, while Amgen routinely obtains patents for its products and technology, the protection offered by its patents and patent applications may be challenged, invalidated or circumvented by its competitors, or Amgen may fail to prevail in present and future intellectual property litigation. Amgen performs a substantial amount of its commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depends on third parties for a portion of its manufacturing activities, and limits on supply may constrain sales of certain of its current products and product candidate development. An outbreak of disease or similar public health threat, such as COVID-19, and the public and governmental effort to mitigate against the spread of such disease, could have a significant adverse effect on the supply of materials for Amgen's manufacturing activities, the distribution of Amgen's products, the commercialization of Amgen's product candidates, and Amgen's clinical trial operations, and any such events may have a material adverse effect on Amgen's product development, product sales, business and results of operations. Amgen relies on collaborations with third parties for the development of some of its product candidates and for the commercialization and sales of some of its commercial products. In addition, Amgen competes with other companies with respect to many of its marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for Amgen's products are supplied by sole third-party suppliers. Certain of Amgen's distributors, customers and payers have substantial purchasing leverage in their dealings with Amgen. The discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on its business and results of operations. Amgen's efforts to collaborate with or acquire other companies, products or technology, and to integrate the operations of companies or to support the products or technology Amgen has acquired, may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of Amgen's systems and Amgen's data. Amgen's stock price may be volatile and may be affected by a number of events. Amgen's business performance could affect or limit the ability of the Amgen Board of Directors to declare a dividend or its ability to pay a dividend or repurchase its common stock. Amgen may not be able to access the capital and credit markets on terms that are favorable to it, or at all.

The scientific information discussed in this news release related to Amgen's product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates.

Cytokinetics 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 GALACTIC-HF; 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 approval of omecamtiv mecarbil by the FDA or any other regulatory agency; the successful marketing and commercialization of omecamtiv mecarbil; Cytokinetics' and its partners' research and development activities; the design, timing, results, significance and utility of preclinical and clinical results; and the properties and potential benefits of Cytokinetics' drug candidates. Such statements are based on management's current expectations and beliefs, 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; the impact of the COVID-19 pandemic on our research and development activities and business operations, Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy; the FDA or foreign regulatory agencies may delay or limit Cytokinetics' or its partners' ability to conduct clinical trials; Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Amgen's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for omecamtiv mecarbil; standards of care may change, rendering Cytokinetics' drug candidates obsolete; competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from its partners, including milestones and royalties on future potential product sales under Cytokinetics' collaboration agreements with such partners. 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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References

1. Pspotka MA, Gottlieb SS, Francis GS et al. Cardiac Calcitropes, Myotropes, and Mitotropes. *JACC*. 2019; 73:2345-53.

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. 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.
4. 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.
5. 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.
6. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. *Lancet* 2018; 392: 1789–858.
7. 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.
8. 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.
9. Roger VL. Epidemiology of Heart Failure. *Circulation Research.* 2013;113:646-659, originally published August 29, 2013. Doi: 10.1161/CIRCRESAHA.113.300268.
10. 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.
11. 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.
12. 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.
13. 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.

