



## Amgen, Cytokinetics and Servier Announce Continuation of GALACTIC-HF Following Planned Interim Analysis

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### Data Monitoring Committee Recommends Phase 3 Clinical Trial of Omecamtiv Mecarbil in Patients With Heart Failure to Continue Without Changes

THOUSAND OAKS, Calif. and SOUTH SAN FRANCISCO, Calif. and SURESNES, France, March 20, 2019 (GLOBE NEWSWIRE) -- Amgen (NASDAQ: AMGN), Cytokinetics, Incorporated (NASDAQ: CYTK) and Servier today announced that the Data Monitoring Committee (DMC) for GALACTIC-HF recently completed the first planned interim analysis, which included consideration of pre-specified criteria for futility. The DMC reviewed data from GALACTIC-HF and recommended that this Phase 3 clinical trial of *omecamtivmecarbil* continue without changes to its conduct.



The futility analysis was triggered once a pre-specified number of cardiovascular deaths had occurred in GALACTIC-HF as stipulated by the trial's protocol. The futility analysis allowed the potential for stopping GALACTIC-HF early had the interim analysis shown a low likelihood of the trial demonstrating a clinically meaningful and statistically significant benefit on the primary endpoint in patients receiving *omecamtivmecarbil*, plus standard of care, compared to patients receiving placebo plus standard of care.

GALACTIC-HF opened to enrollment in late 2016 and is designed to enroll approximately 8,000 patients in over 35 countries who are either currently hospitalized for a primary reason of heart failure or have had a hospitalization or admission to an emergency room for heart failure within one year prior to screening. The trial is designed to evaluate whether treatment with *omecamtivmecarbil*, when added to standard of care, reduces the risk of heart failure events (heart failure hospitalization and other urgent treatment for heart failure) and cardiovascular (CV) death in patients with chronic heart failure with reduced ejection fraction. To date, over 7,000 patients have been enrolled in GALACTIC-HF and completion of enrollment is expected in the first half of 2019.

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

*Omecamtivmecarbil* is a novel, selective cardiac myosin activator that binds to the catalytic domain of myosin. Preclinical research has shown that cardiac myosin activators increase cardiac contractility without affecting intracellular myocyte calcium concentrations or myocardial oxygen consumption.<sup>1-3</sup> 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.

*Omecamtivmecarbil* 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. *Omecamtivmecarbil* is the subject of a comprehensive Phase 3 clinical trials program comprised of GALACTIC-HF (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure), a large, Phase 3 global cardiovascular outcomes study being conducted by Amgen in collaboration with Cytokinetics and Servier, 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 *omecamtivmecarbil* compared to placebo on exercise capacity, being conducted by Cytokinetics in collaboration with Amgen, with funding and strategic support from Servier.

#### About Heart Failure

Heart failure is a grievous condition that affects more than 26 million people worldwide<sup>4,5</sup> about half of whom have reduced left ventricular function.<sup>6,7</sup> It is the leading cause of hospitalization and readmission in people age 65 and older.<sup>8,9</sup> Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor.<sup>10</sup> 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.<sup>11,12</sup>

#### 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. *Omecamtivmecarbil* is being developed by Amgen in collaboration with Cytokinetics, with funding and strategic support from Servier. Amgen holds an exclusive, worldwide license to *omecamtivmecarbil* 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 *omecamtivmecarbil* in exchange for increased royalties from Amgen on worldwide sales of *omecamtivmecarbil* 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 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](http://www.amgen.com) and follow us on [www.twitter.com/amgen](https://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 best-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 Phase 3 clinical trials program 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 collaborating with Astellas Pharma Inc. (Astellas) to develop *reldesemtiv*, a fast skeletal muscle troponin activator (FSTA). *Reldesemtiv* has been granted orphan drug designation by the FDA for the potential treatment of spinal muscular atrophy. *Reldesemtiv* was the subject of a Phase 2 clinical study in patients with spinal muscular atrophy which showed increases in measures of endurance and stamina consistent with the mechanism of action. *Reldesemtiv* is currently the subject of a Phase 2 clinical trial in patients with amyotrophic lateral sclerosis. Astellas holds an exclusive worldwide license to develop and commercialize *reldesemtiv*. 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 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](http://www.cytokinetics.com) and follow us on [Twitter](https://www.twitter.com/cytokinetics), [LinkedIn](https://www.linkedin.com/company/cytokinetics), [Facebook](https://www.facebook.com/cytokinetics) and [YouTube](https://www.youtube.com/channel/UC8vYqKqKqKqKqKqKqKqKqKq).

#### **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 149 countries and a turnover of 4.2 billion euros in 2018, Servier employs 22,000 people worldwide. Entirely independent, the Group reinvests 25% of its turnover (excluding generics) in research and development and uses all its profits for development. Corporate growth is driven by Servier's constant search for innovation 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](http://www.servier.com).

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#### **Amgen Forward-Looking Statement**

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 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 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. 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 manufacturing 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. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our 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 acquire other companies or products and to integrate the operations of companies 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 Cytokinetics' and its partners' research and development activities; the timing of enrollment of patients in Cytokinetics' and its partners' clinical trials; 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, 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; patient enrollment for or conduct of clinical trials may be difficult or delayed; 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; and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Astellas' decisions with respect to the design, initiation, conduct, timing and continuation of development activities for *reldesemtiv*; 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

- <sup>1</sup> Planelles-Herrero VJ, Hartman JJ, Robert-Paganin J. et al. Mechanistic and structural basis for activation of cardiac myosin force production by omeamtiv mecarbil. *Nat Commun.* 2017;8:190.
- <sup>2</sup> 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.
- <sup>3</sup> 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.
- <sup>4</sup> Savarese G and Lund LH. Global Public Health Burden of Heart Failure. *Cardiac Failure Review* 2017;3 (1): 7-11.
- <sup>5</sup> Ponikowski P, Anker SD, AlHabib KF, et al. Heart failure: preventing disease and death worldwide. *ESC Heart Failure* 2014;1:4–25.
- <sup>6</sup> 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.
- <sup>7</sup> 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.
- <sup>8</sup> Roger VL. Epidemiology of Heart Failure. *Circulation Research.* 2013;113:646-659, originally published August 29, 2013. Doi: 10.1161/CIRCRESAHA.113.300268.
- <sup>9</sup> 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.
- <sup>10</sup> 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.
- <sup>11</sup> 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.
- <sup>12</sup> Rogers VL, Weston SA, Redfield MM, et al. Trends in Heart Failure Incidence and Survival in a Community-Based Population. *JAMA.* 2004;292:344-350.

Source: Cytokinetics, Incorporated