# Amgen Announces New Analyses Of High-Risk Patient Subgroups From Repatha® (evolocumab) Cardiovascular Outcomes Study At AHA Scientific Sessions 2017

November 6, 2017

**Late-Breaking Repatha Presentations Assess Impact on Peripheral Artery Disease and Heart Attack Patients**

THOUSAND OAKS, Calif., Nov. 6, 2017 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced new analyses will be presented from the Repatha® (evolocumab) cardiovascular outcomes study, including analyses investigating the efficacy of Repatha in high-risk patients with peripheral artery disease (PAD) and those who have experienced a prior heart attack. In total, five distinct analyses from the Repatha cardiovascular outcomes study (FOURIER), including two accepted for late-breaker scientific sessions, will be presented at the American Heart Association (AHA) Scientific Sessions 2017 in Anaheim, Calif., Nov. 11-15.

"Amgen is transforming medicine to combat the growing public health crisis of cardiovascular disease," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "These new Repatha cardiovascular outcomes study analyses will help clinicians further understand the role of Repatha and identify appropriate patients for whom it can maximize benefit on top of current statin therapy."

Full listing of Amgen-related abstracts at AHA Scientific Sessions 2017 include:

**Repatha**

**Late-Breaking Science Sessions (Session: LBS.02)**

- **Evolocumab and Outcomes in Patients with Peripheral Artery Disease**
  Outcomes – Late-Breaking Science in Prevention; Monday, Nov. 13, 9:36-9:43 a.m. PT
- **Clinical Benefit of Evolocumab in Patients with a History of MI: An Analysis from FOURIER**
  Outcomes – Late-Breaking Science in Prevention; Monday, Nov. 13, 9:43-9:50 a.m. PT

**Oral Sessions (Session: AC.AOS.821)**

- **Reduction in Total Cardiovascular Events with the PCSK9 Inhibitor Evolocumab in Patients with Cardiovascular Disease in the FOURIER Trial**
  Outcomes – Lipid-Lowering Trials New Analyses; Monday, Nov. 13, 9:30-9:40 a.m. PT
- **Characterization of Types and Sizes of Myocardial Infarction Reduced with Evolocumab in FOURIER**
  Outcomes – Lipid-Lowering Trials – New Analyses; Monday, Nov. 13, 9:45-9:55 a.m. PT
- **Predictors of Residual Plaque Progression Despite Achieving Low Levels of LDL-C with the PCSK9 Inhibitor, Evolocumab (GLAGOV)**
  Lipid Trials and Clinical Management (PR.AOS.876); Monday, Nov. 13, 5:30-5:40 p.m. PT

**Poster Sessions**

- **Work Productivity Losses in the Year Following Acute Coronary Syndrome or Stroke: Interim Results of a Multi-Country Survey in Europe**
  Quality Assessments in Big Data (QU.APS.03); Sunday, Nov. 12, 3:15-4:30 p.m. PT
- **Trends in Statin Use Among Adults with and Without HIV**
  Distinct Populations (EP.APS.06); Monday, Nov. 13, 10:30-11:45 a.m. PT
- **Atherothrombotic Risk Stratification and Magnitude of Benefit of Evolocumab in FOURIER**
  Management and Outcomes in Chronic CHD (AC.APS.09); Monday, Nov. 13, 12:45-2 p.m. PT
- **Cardiovascular Event Rates According to Low-Density Lipoprotein Cholesterol Level Among Statin-Treated Patients with Existing Cardiovascular Disease**
  Epidemiology, Big Data and Precision Medicine: General Topics II (EP.APS.11); Tuesday, Nov. 14, 10:30-11:45 a.m. PT
- **Regression of Coronary Atherosclerosis with the PCSK9 Inhibitor Evolocumab in Patients with Coronary Artery Disease and Diabetes (GLAGOV)**
  Diabetes Mellitus and CVD: Prevention and Management (CM.APS.03); Tuesday, Nov. 14, 10:30-11:45 a.m. PT
- **Cardiovascular Event Rates After Myocardial Infarction or Ischemic Stroke in Older Medicare Patients**
  Epidemiology and Population Studies (EP.APS.09); Tuesday, Nov. 14, 10:30-11:45 a.m. PT

- **Gender Disparities in Use of Cardiologist Care**
  Race, Sex, SES: Disparities in Cardiovascular Care (WS.APS.04); Tuesday, Nov. 14, noon-1:15 p.m. PT

**Omecamtiv mecarbil**

- **Treatment with Omecamtiv Mecarbil, a Cardiac Myosin Activator, Improves NT-proBNP in Patients with Chronic Heart Failure: A Responder Analysis from COSMIC-HF**
  A Whirlwind Tour of Insights into CHF and Cardiomyopathy; Monday, Nov. 13, 11:10-11:15 a.m. PT

**Repatha Cardiovascular Outcomes (FOURIER) Study Design**
The 27,564-patient Repatha cardiovascular outcomes study, FOURIER (Further Cardiovascular OUtcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk), was a multinational Phase 3 randomized, double-blind, placebo-controlled trial, designed to evaluate whether treatment with Repatha in combination with statin therapy compared to placebo plus statin therapy reduces cardiovascular events. The primary endpoint was time to cardiovascular death, MI, stroke, hospitalization for unstable angina, or coronary revascularization. The key secondary endpoint was the time to cardiovascular death, MI or stroke.

Eligible patients with high cholesterol (LDL-C ≥70 mg/dL or non-high-density lipoprotein cholesterol [non-HDL-C] ≥100 mg/dL) and clinically evident atherosclerotic cardiovascular disease at more than 1,200 study locations around the world were randomized to receive Repatha subcutaneous 140 mg every two weeks or 420 mg monthly plus optimized statin dose; or placebo subcutaneous every two weeks or monthly plus optimized statin dose. Optimized statin therapy was defined as at least atorvastatin 20 mg or equivalent daily with a recommendation for at least atorvastatin 40 mg or equivalent daily where approved. The study was event driven and continued until 1,630 patients experienced a key secondary endpoint.

**GLAGOV Study Design**
GLAGOV (GLobal Assessment of Plaque ReGression with a PCSK9 AntibOdy as Measured by IntraVascular Ultrasound) is a Phase 3, multicenter, double-blind, randomized, placebo-controlled trial designed to evaluate the effect of Repatha on the change in burden of coronary artery disease (CAD) in 968 patients undergoing clinically indicated coronary angiogram and on optimized background statin therapy.

Patients were required to have been treated with a stable statin dose for at least four weeks and to have a LDL-C ≥80 mg/dL or between 60 and 80 mg/dL with one major cardiovascular risk factor (defined as non-coronary atherosclerotic vascular disease, myocardial infarction or hospitalization for unstable angina in the preceding two years or type 2 diabetes mellitus) or three minor cardiovascular risk factors (defined as current cigarette smoking, hypertension, low levels of HDL cholesterol, family history of premature coronary heart disease, high sensitivity C-reactive protein (hs-CRP) ≥2 mg/L or age ≥50 years in men and 55 years in women).

Patients were randomized 1:1 into two treatment groups to either receive monthly Repatha 420 mg or placebo subcutaneous injections. Optimized statin therapy was defined as at least atorvastatin 20 mg daily or equivalent, titrated to achieve LDL-C reduction per regional guidelines. Highly effective statin therapy (equivalent to atorvastatin 40 mg daily or higher) was recommended for all patients. Those patients with LDL-C >100 mg/dL not taking highly effective statin therapy, required investigators' attestation as to why such doses were not appropriate. The primary endpoint was change in percent atheroma volume (PAV) from baseline to week 78 compared to placebo, as determined by intravascular ultrasound (IVUS). IVUS is a high-resolution imaging tool that allows for the quantification of coronary atheroma in the coronary arteries.

Secondary endpoints included PAV regression (any reduction from baseline); change in total atheroma volume (TAV) from baseline to week 78; and regression (any reduction from baseline) in TAV.

**COSMIC-HF Trial Design**
COSMIC-HF (Chronic Oral Study of Myosin Activation to Increase Contractility in Heart Failure) was a double-blind, randomized, placebo-controlled, multicenter, Phase 2 trial designed to evaluate an oral formulation of omecamtiv mecarbil in chronic heart failure patients with reduced ejection fraction. The trial consisted of two parts, a dose escalation phase and a larger and longer expansion phase. The dose escalation phase, which completed in 2013, assessed the pharmacokinetics and tolerability of three oral modified-release formulations of omecamtiv mecarbil and was used to select one formulation for further evaluation in the expansion phase. In the dose escalation phase, 96 patients were randomized 1:1:1:1 to placebo or one of three oral modified-release formulations of omecamtiv mecarbil in two cohorts (25 mg twice daily or 50 mg twice daily). Each patient cohort was followed for 35 days.

The expansion phase evaluated 448 chronic heart failure patients with reduced ejection fraction who were dosed with the selected oral formulation of omecamtiv mecarbil for 20 weeks and followed for a total of 24 weeks. Patients were randomized 1:1:1 to receive either placebo or treatment with omecamtiv mecarbil 25 mg twice daily or 25 mg with dose escalation to 50 mg twice daily, depending on plasma concentrations of omecamtiv mecarbil after two weeks of treatment. The pharmacokinetic-based dose titration strategy was designed to maintain patient exposure to omecamtiv mecarbil in a targeted plasma concentration range; approximately 60 percent of patients in the dose titration group were escalated to a dose of 50 mg twice daily.

The primary endpoints for the expansion phase were to assess the maximum and pre-dose plasma concentration of omecamtiv mecarbil. The secondary endpoints were to assess changes from baseline in systolic ejection time, stroke volume, left ventricular end-systolic diameter, left ventricular end-diastolic diameter, heart rate and N-terminal pro-brain natriuretic peptide (a biomarker associated with the severity of heart failure) at week 20, as well as the safety and tolerability of omecamtiv mecarbil including incidence of adverse events from baseline to week 24.

COSMIC-HF was not designed to assess the impact of omecamtiv mecarbil on cardiovascular outcomes in heart failure patients.

COSMIC-HF was conducted by Amgen in collaboration with Cytokinetics.

**About Repatha® (evolocumab)**
Repatha® (evolocumab) is a human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9). Repatha binds to PCSK9 and inhibits circulating PCSK9 from binding to the low-density lipoprotein (LDL) receptor (LDLR), preventing PCSK9-mediated LDLR degradation and permitting LDLR to recycle back to the liver cell surface. By inhibiting the binding of PCSK9 to LDLR, Repatha increases the number of LDLRs available to clear LDL from the blood, thereby lowering LDL-C levels.[1]

Repatha is approved in more than 50 countries, including the U.S., Japan, Canada and in all 28 countries that are members of the European Union. Applications in other countries are pending.

**U.S. Repatha Indication**

Repatha® is indicated as an adjunct to diet and:

- Maximally tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C)
- Other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C

The effect of Repatha® on cardiovascular morbidity and mortality has not been determined.

The safety and effectiveness of Repatha® have not been established in pediatric patients with HoFH who are younger than 13 years old.

The safety and effectiveness of Repatha® have not been established in pediatric patients with primary hyperlipidemia or HeFH.

**Important U.S. Safety Information**

**Contraindication:** Repatha® is contraindicated in patients with a history of a serious hypersensitivity reaction to Repatha®.

**Allergic reactions:** Hypersensitivity reactions (e.g. rash, urticaria) have been reported in patients treated with Repatha®, including some that led to discontinuation of therapy. If signs or symptoms of serious allergic reactions occur, discontinue treatment with Repatha®, treat according to the standard of care, and monitor until signs and symptoms resolve.

**Adverse reactions:** The most common adverse reactions (>5% of Repatha®-treated patients and more common than placebo) were: nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions.

In a 52-week trial, adverse reactions led to discontinuation of treatment in 2.2% of Repatha®-treated patients and 1% of placebo-treated patients. The most common adverse reaction that led to Repatha® treatment discontinuation and occurred at a rate greater than placebo was myalgia (0.3% versus 0% for Repatha® and placebo, respectively).

Adverse reactions from a pool of the 52-week trial and seven 12-week trials: Local injection site reactions occurred in 3.2% and 3.0% of Repatha®-treated and placebo-treated patients, respectively. The most common injection site reactions were erythema, pain, and bruising. The proportions of patients who discontinued treatment due to local injection site reactions in Repatha®-treated patients and placebo-treated patients were 0.1% and 0%, respectively.

Allergic reactions occurred in 5.1% and 4.7% of Repatha®-treated and placebo-treated patients, respectively. The most common allergic reactions were rash (1.0% versus 0.5% for Repatha® and placebo, respectively), eczema (0.4% versus 0.2%), erythema (0.4% versus 0.2%), and urticaria (0.4% versus 0.1%).

Neurocognitive events were reported in less than or equal to 0.2% in Repatha®-treated and placebo-treated patients.

In a pool of placebo- and active-controlled trials, as well as open-label extension studies that followed them, a total of 1,988 patients treated with Repatha® had at least one LDL-C value <25 mg/dL. Changes to background lipid-altering therapy were not made in response to low LDL-C values, and Repatha® dosing was not modified or interrupted on this basis. Although adverse consequences of very low LDL-C were not identified in these trials, the long-term effects of very low levels of LDL-C induced by Repatha® are unknown.

Musculoskeletal adverse reactions were reported in 14.3% of Repatha®-treated patients and 12.8% of placebo-treated patients. The most common adverse reactions that occurred at a rate greater than placebo were back pain (3.2% versus 2.9% for Repatha® and placebo, respectively), arthralgia (2.3% versus 2.2%), and myalgia (2.0% versus 1.8%).

**Homozygous Familial Hypercholesterolemia (HoFH):** In 49 patients with homozygous familial hypercholesterolemia studied in a 12-week, double-blind, randomized, placebo-controlled trial, 33 patients received 420 mg of Repatha® subcutaneously once monthly. The adverse reactions that occurred in at least 2 (6.1%) Repatha®-treated patients and more frequently than in placebo-treated patients, included upper respiratory tract infection (9.1% versus 6.3%), influenza (9.1% versus 0%), gastroenteritis (6.1% versus 0%), and nasopharyngitis (6.1% versus 0%).

**Immunogenicity:** Repatha® is a human monoclonal antibody. As with all therapeutic proteins, there is a potential for immunogenicity with Repatha®.

Please contact Amgen Medinfo at 800-77-AMGEN (800-772-6436) or 844-REPATHA (844-737-2842) regarding Repatha® availability or find more information, including full Prescribing Information, at www.amgen.com and www.Repatha.com.

**About Omecamtiv Mecarbil**
Omecamtiv mecarbil is a novel cardiac myosin activator. 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. Cardiac myosin activators are thought to accelerate the rate-limiting step of the myosin enzymatic cycle and shift the enzymatic cycle in favor of the force-producing state. Preclinical research has shown that cardiac myosin activators increase contractility in the absence of changes in intracellular calcium in cardiac myocytes.[2,3,4]

Omecamtiv mecarbil is being developed by Amgen in collaboration with Cytokinetics. Amgen holds an exclusive, worldwide license to omecamtiv

mecarbil and related compounds, subject to Cytokinetics' specified development and commercialization rights. 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 in the Cardiovascular Therapeutic Area**
Building on more than three decades of experience in developing biotechnology medicines for patients with serious illnesses, Amgen is dedicated to addressing important scientific questions to advance care and improve the lives of patients with cardiovascular disease, the leading cause of morbidity and mortality worldwide.[5] Amgen's research into cardiovascular disease, and potential treatment options, is part of a growing competency at Amgen that utilizes human genetics to identify and validate certain drug targets. Through its own research and development efforts, as well as partnerships, Amgen is building a robust cardiovascular portfolio consisting of several approved and investigational molecules in an effort to address a number of today's important unmet patient needs, such as high cholesterol and heart failure.

**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 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 one of the world's leading independent biotechnology companies, 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.

**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 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 our 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 we project. 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 us to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. We develop 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 we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products, including our devices, after they are on the market.

Our results may be affected by our 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 our products and global economic conditions. In addition, sales of our 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, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. The discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to acquire other companies or products and to integrate the operations of companies we have acquired may not be successful. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all. We are increasingly dependent on information technology systems, infrastructure and data security. Our stock price is volatile and may be affected by a number of events. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock.

The scientific information discussed in this news release relating to new indications is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration or European Commission for the products. The products are not approved for the investigational use(s) discussed in this news release, and no conclusions can or should be drawn regarding the safety or effectiveness of the products for these uses.

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