New Detailed Data From Phase 3 Study Show Amgen's Repatha™ (Evolocumab) In Combination With Statins Reduced LDL-C By 67-76 Percent Compared To Placebo In Japanese Patients With High Cardiovascular Risk And High Cholesterol

March 14, 2015

Data From PCSK9 Inhibitor Study Support Regulatory Filing in Japan

THOUSAND OAKS, Calif., March 14, 2015 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced new detailed data from the Phase 3 YUKAWA-2 study evaluating Repatha™ (evolocumab), a novel investigational cholesterol-lowering medication, in Japanese patients with high cardiovascular risk and high cholesterol. Data from the study showed subcutaneous Repatha 140 mg every two weeks or 420 mg monthly, compared to placebo, in combination with different daily doses of atorvastatin, reduced low-density lipoprotein cholesterol (LDL-C) by 67 to 76 percent from baseline at week 12 and at the mean of weeks 10 and 12. The data were presented at the American College of Cardiology's 64th Annual Scientific Session (ACC.15).

In the YUKAWA-2 study, the most common adverse events that occurred in greater than 2 percent of the Repatha group were nasopharyngitis (16.8 percent Repatha; 17.8 percent placebo), gastroenteritis (3.0 percent Repatha; 1.0 percent placebo) and pharyngitis (2.5 percent Repatha; 2.5 percent placebo).

"The positive results from this study in Japan add to the consistent findings we have seen with Repatha across patient populations in our comprehensive clinical program," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Statins are an important therapy for patients with high cholesterol and adding Repatha may help lower their LDL cholesterol levels when statins are not sufficient. We look forward to working with regulatory authorities in Japan to bring this new investigational medication to patients."

Repatha is an investigational fully human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9), a protein that reduces the liver's ability to remove LDL-C, or "bad" cholesterol, from the blood.[1] In Japan, LDL-C levels are not adequately controlled for many high-risk patients taking statins, nearly half of whom have not reached their LDL-C goal.[2,3]

"Statins are a cornerstone of treatment for people with high cholesterol who are unable to lower their LDL cholesterol to appropriate levels despite efforts to improve diet and exercise," said Arihiro Kiyosue, Department of Cardiovascular Medicine, Graduate School of Medicine, University of Tokyo, Japan, and Tokyo-Eki Center-building Clinic, Tokyo, Japan, and investigator for the YUKAWA-2 study. "We are encouraged by the results from the Phase 3 YUKAWA-2 study, which show that adding evolocumab to stable statin therapy in high-risk patients further reduced LDL cholesterol."

High cholesterol is the most common form of dyslipidemia, which is an abnormality of cholesterol and/or fats in the blood.[4,5] There are approximately 300 million cases of dyslipidemia in the U.S., Japan and Western Europe.[6]

YUKAWA-2 Study Design

YUKAWA-2 (StudY of LDL-Cholesterol Reduction Using a Monoclonal PCSK9 Antibody in Japanese Patients With Advanced Cardiovascular Risk) is a Phase 3, multicenter, double-blind, randomized, placebo-controlled trial designed to evaluate the safety, tolerability and efficacy of Repatha ™ (evolocumab) in 404 Japanese patients with high cardiovascular risk based on the Japan Atherosclerosis Society guidelines[2] and with hyperlipidemia or mixed dyslipidemia (LDL-C ≥100 mg/dL). Patients were randomized to one of eight treatment groups in a two-step randomization. Eligible patients were initially randomized to one of the following background therapies: atorvastatin 5 mg daily or atorvastatin 20 mg daily and entered a four-week lipid stabilization period. At completion of lipid stabilization, patients were then randomized to one of four treatment arms: Repatha 140 mg every two weeks, Repatha 420 mg monthly, subcutaneous placebo every two weeks or subcutaneous placebo monthly. The co-primary endpoints were the percent reduction from baseline in LDL-C at week 12 and the mean percent reduction from baseline in LDL-C at weeks 10 and 12. Co-secondary efficacy endpoints included means at weeks 10 and 12 and at week 12 for the following: LDL-C <70 mg/dL; absolute change from baseline in LDL-C; and the percentage change from baseline in non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (ApoB), total cholesterol (TC), TC/HDL-C ratio, ApoB/apolipoprotein A1 (ApoA1) ratio, lipoprotein(a), triglycerides, HDL-C and very low-density lipoprotein cholesterol (VLDL-C).

Amgen Webcast Investor Call

Amgen will host a webcast investor call on Monday, March 16, at 1 p.m. PT. Sean E. Harper, M.D., executive vice president of Research and Development at Amgen, along with members of Amgen's clinical development team, will participate in the call to discuss Amgen's cardiovascular program, including Repatha data presented at ACC.15.

Live audio of the investor meeting will be simultaneously broadcast over the Internet and will be available to members of the news media, investors and the general public.

The webcast, as with other selected presentations regarding developments in Amgen's business given by management at certain investor and medical conferences, can be found on Amgen's website, www.amgen.com, under Investors. Information regarding presentation times, webcast availability and webcast links are noted on Amgen's Investor Relations Events Calendar. The webcast will be archived and available for replay for at least 90 days after the event.

About Repatha ™(Evolocumab)

Repatha ™(evolocumab) is a fully human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9).[1] PCSK9 is a protein that targets LDL receptors for degradation and thereby reduces the liver's ability to remove LDL-C, or "bad" cholesterol, from the blood.[7] Repatha, being developed by Amgen scientists, is designed to bind to PCSK9 and inhibit PCSK9 from binding to LDL receptors on the liver surface. In the absence of PCSK9, there are more LDL receptors on the surface of the liver to remove LDL-C from the blood.[1]

The FDA has provisionally approved the trade name Repatha.

Repatha is developed in Japan by Amgen Astellas BioPharma K.K., a joint venture between Amgen and Astellas Pharma Inc., a pharmaceutical company headquartered in Tokyo, Japan.

About PROFICIO: Repatha ™(Evolocumab) Clinical Trial Program

PROFICIO, which stands for the Program to Reduce LDL-C and Cardiovascular Outcomes Following Inhibition of PCSK9 In Different POpulations, is a large and comprehensive clinical trial program evaluating Repatha ™(evolocumab) in 22 clinical trials, with a combined planned enrollment of approximately 35,000 patients.

The Phase 3 program includes 16 trials to evaluate Repatha administered every two weeks and monthly in multiple patient populations, including in combination with statins in patients with hyperlipidemia (LAPLACE-2 and YUKAWA-2); in patients with hyperlipidemia who cannot tolerate statins (GAUSS-2 and GAUSS-3); as a stand-alone treatment in patients with hyperlipidemia (MENDEL-2); in patients whose elevated cholesterol is caused by genetic disorders called heterozygous (RUTHERFORD-2 and TAUSSIG) and homozygous (TESLA and TAUSSIG) familial hypercholesterolemia; the effects of Repatha on lipoprotein metabolism (FLOREY); and the administration of Repatha in statin-treated hyperlipidemic patients (THOMAS-1 and THOMAS-2).

Five ongoing studies in the Repatha Phase 3 program will provide long-term safety and efficacy data. These include FOURIER (Further Cardiovascular OUtcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk), which will assess whether treatment with Repatha in combination with statin therapy compared to placebo and statin therapy reduces recurrent cardiovascular events in approximately 27,500 patients with cardiovascular disease; EBBINGHAUS (Evaluating PCSK9 Binding AntiBody Influence oN CoGnitive HeAlth in High CardiovascUlar Risk Subjects), which will evaluate the effect of Repatha on cognitive function in a subset of patients enrolled in FOURIER; OSLER-2 (Open Label Study of Long TERm Evaluation Against LDL-C Trial-2) in patients with high cholesterol who completed any of the Phase 3 studies; GLAGOV (GLobal Assessment of Plaque ReGression with a PCSK9 AntibOdy as Measured by IntraVascular Ultrasound), which will determine the effect of Repatha on coronary atherosclerosis in approximately 950 patients undergoing cardiac catheterization; and TAUSSIG (Trial Assessing Long Term USe of PCSK9 Inhibition in Subjects with Genetic LDL Disorders), which will assess the long-term safety and efficacy of Repatha on LDL-C in patients with severe familial hypercholesterolemia including patients with homozygous familial hypercholesterolemia. The DESCARTES (Durable Effect of PCSK9 Antibody CompARed wiTh PlacEbo Study) study, a long-term safety and efficacy trial in patients with hyperlipidemia at risk for cardiovascular disease, has been completed.

About Amgen's Commitment to Cardiovascular Disease
Amgen is dedicated to addressing important scientific questions in order to advance care and improve the lives of patients with cardiovascular disease. Through its own research and development efforts and innovative partnerships, Amgen has built a robust cardiology pipeline consisting of several 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 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 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 management's current expectations and beliefs and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. 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 (SEC) reports filed by Amgen, including Amgen's most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen's most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Amgen is providing this information as of March 14, 2015, and expressly disclaims any duty to update information contained in this news release.

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. 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 after they are on the market. Our business may be impacted by government investigations, litigation and products liability claims. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products are affected by the reimbursement policies imposed by third-party payors, 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 as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government

and others' regulations and reimbursement policies may affect the development, usage and pricing of our products. In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, 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 and there can be no guarantee of our ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, 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 integrate the operations of companies we have acquired may not be successful. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plan. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or their ability to pay a dividend or repurchase our common stock.

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

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References

1. Amgen Data on File, Investigator Brochure.
2. Teramoto T, Sasaki J, Ishibashi S, et al. Executive Summary of the Japan Atherosclerosis Society (JAS) Guidelines for the Diagnosis and Prevention of Atherosclerotic Cardiovascular Diseases in Japan – 2012 version. *J Atheroscler Thromb.* 2013;20(6):517-523.
3. Teramoto T, Kashiwagi A, Ishibashi S, Daida H. Cross-Sectional Survey to Assess the Status of Lipid Management in High-Risk Patients With Dyslipidemia: Clinical Impact of Combination Therapy With Ezetimibe. *Current Therapeutic Research*. 2013;73(1-2).
4. World Health Organization. Quantifying Selected Major Risks to Health. In: The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Chapter 4: Geneva: World.
5. Merck Manuals website. http://www.merckmanuals.com/professional/endocrine_and_metabolic_disorders/lipid_disorders/dyslipidemia.html. Accessed February 2015.
6. National Institute of Health (2009). Federal Register Volume 74 (250). Washington, DC: U.S. Government Printing Office. http://www.gpo.gov/fdsys/pkg/FR-2009-12-31/html/E9-31072.htm. Accessed February 2015.
7. Abifadel M et al. Mutations in PCSK9 cause autosomal dominant hypercholesterolemia. *Nat Genet*. 2003;34:154-156.

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