Amgen Publishes Safety Analysis Of Investigational Cholesterol-Lowering Medication Repatha™ (evolocumab) In The New England Journal of Medicine

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Analysis From Prespecified Exploratory Endpoints Presented in Late-Breaking Session at ACC.15 Showed Repatha Plus Standard of Care Lowered Cardiovascular Events

Amgen to Webcast Investor Call at ACC.15

THOUSAND OAKS, Calif., March 15, 2015 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced one-year data from prespecified exploratory endpoints of adjudicated cardiovascular events in the Phase 2 (OSLER-1) and Phase 3 (OSLER-2) open-label extension studies of Repatha ™ (evolocumab), a novel investigational low-density lipoprotein cholesterol (LDL-C)-lowering medication. These data were presented today at a Late-Breaking Clinical Trial session at the American College of Cardiology's 64th Annual Scientific Session (ACC.15) and published in the *New England Journal of Medicine.* A two-year analysis of Repatha safety and tolerability data from the longest proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor trial to date (OSLER-1) was also presented.

Data from prespecified exploratory endpoints in the ongoing open-label OSLER-1 and OSLER-2 studies showed Repatha plus standard of care (SOC) treatment reduced adjudicated cardiovascular events (0.95 percent Repatha plus SOC; 2.18 percent SOC) over a one-year analysis period. Adverse events (AEs) (≥1 percent in the Repatha plus SOC group and more frequent in the Repatha plus SOC group by at least 1 percent) included arthralgia, headache, pain in extremity and fatigue. The cardiovascular events analysis comprises exploratory findings from the ongoing open-label OSLER studies. Repatha plus SOC treatment reduced LDL-C by 61 percent compared to SOC.

"We are excited to present several data analyses at ACC.15 from the Repatha clinical trial program, including an analysis of cardiovascular events and safety data from the longest PCSK9 inhibitor trial to date," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The clinical data are encouraging, and we look forward to seeing the results from our cardiovascular outcomes trial, FOURIER, which was designed to investigate whether there is a substantial reduction in the occurrence of major cardiovascular events with the use of Repatha. We continue to work with regulatory agencies to make Repatha available to patients."

Effect of Repatha on Adjudicated Cardiovascular Events

The OSLER-1 and OSLER-2 trials are ongoing open-label extension studies designed to characterize long-term effects of Repatha. The trials enrolled 4,465 patients who had completed one of 12 Phase 2 and 3 Repatha studies, 2,976 of whom were randomized to subcutaneous Repatha 140 mg every two weeks or 420 mg monthly plus SOC therapy and 1,489 were randomized to SOC alone over one year. The median LDL-C was 120 mg/dL at parent study baseline; approximately 70 percent of patients were on a statin at the start of the extension studies. Compared to SOC alone, Repatha plus SOC reduced adjudicated cardiovascular events (death, myocardial infarction, unstable angina requiring hospitalization, coronary revascularization, stroke and transient ischemic attack or heart failure requiring hospitalization) compared to SOC alone (0.95 percent Repatha plus SOC vs. 2.18 percent SOC over one year), with a consistent effect on death, coronary and cerebrovascular events as well as by subgroups (e.g., age, sex, baseline LDL-C, statin use, National Cholesterol Education Program [NCEP] risk).

Adverse events with a frequency of at least 1 percent in the Repatha plus SOC arm and that were more frequent with Repatha plus SOC by at least 1 percent included arthralgia (4.6 percent Repatha plus SOC; 3.2 percent SOC), headache (3.6 percent Repatha plus SOC; 2.1 percent SOC), pain in extremity (3.3 percent Repatha plus SOC; 2.1 percent SOC) and fatigue (2.8 percent Repatha plus SOC; 1.0 percent SOC). Adverse events of interest included muscle-related AEs (6.4 percent Repatha plus SOC; 6.0 percent SOC), injection site reactions (4.3 percent Repatha plus SOC; N/A SOC) and neurocognitive events (0.9 percent Repatha plus SOC; 0.3 percent SOC). Compared to SOC alone, Repatha plus SOC reduced LDL-C by 61 percent to a median of 48 mg/dL. In this analysis, median study exposure for the first year of the extension studies was 11.1 months.

"Data analysis from the OSLER studies show that evolocumab consistently reduced LDL cholesterol over the one-year period and reduced the rate of cardiovascular events when added to standard of care," said Marc Sabatine, M.D., chairman of TIMI Study Group, and a senior physician in the Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston. "We look forward to the results of the ongoing 27,500-patient dedicated cardiovascular outcomes study, FOURIER."

Two-Year Safety and Tolerability Analysis

Data from the OSLER-1 study showed Repatha maintained its efficacy over a two-year period and no safety risk was identified. The study, which began in October 2011, randomized 1,104 patients who completed short-term, double-blind, controlled Repatha studies to receive SOC (n=370) or SOC plus open-label Repatha 420 mg monthly (n=734) for one year. After the first year, all patients received monthly Repatha plus SOC. At the end of year two, 590 patients were still receiving Repatha, showing a persistence rate of 80 percent. Of the patients on Repatha over the entire two-year period, 33 patients (4.5 percent) discontinued use due to an AE. Safety and tolerability were comparable regardless of achieved LDL-C level. Low-density lipoprotein cholesterol-lowering was sustained for more than two years, with a reduction of 54 percent at week 52 and 52 percent at week 124.

"We are pleased to see that over two years, evolocumab showed a safety and efficacy profile in hypercholesterolemic patients consistent with what we've seen in previous studies," said Michael J. Koren, M.D., investigator for the OSLER-1 study and chief executive officer of the Jacksonville Center for Clinical Research, Jacksonville, Fla. "We are highly encouraged by the data and will continue to evaluate the efficacy and safety profile of evolocumab over time in patients, who, despite currently available therapies, are unable to adequately reduce their LDL cholesterol levels."

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 Cholesterol
High cholesterol, particularly elevated LDL-C, is the most common form of dyslipidemia, which is an abnormality of cholesterol and/or fats in the blood.[1,2] Elevated LDL-C is recognized as a major risk factor for cardiovascular disease.[3,4] Familial hypercholesterolemia (FH) is an inherited condition caused by genetic mutations which lead to high levels of LDL-C at an early age,[5] and it is estimated that less than one percent of people with FH (heterozygous and homozygous forms) in the U.S. are diagnosed.[6]

About Repatha ™(evolocumab)
Repatha ™(evolocumab) is a fully human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9).[7] 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.[8] 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.[7]

The FDA has provisionally approved the trade name Repatha.

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 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 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.

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 15, 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), and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates.

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References

1. World Health Organization. Quantifying Selected Major Risks to Health. In: The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva. 2002:49-97.
2. Merck Manuals website. http://www.merckmanuals.com/professional/endocrine_and_metabolic_disorders/lipid_disorders/dyslipidemia.html. Accessed February 2015.
3. American Heart Association (2012). Why cholesterol matters. http://www.heart.org/HEARTORG/Conditions/Cholesterol/WhyCholesterolMatters/Why-Cholesterol-Matters_UCM_001212_Article.jsp. Accessed February 2015.
4. World Health Organization. Global status report on noncommunicable diseases 2010. Geneva, 2011.
5. National Human Genome Research Institute. Learning About Familial Hypercholesterolemia. http://www.genome.gov/25520184. Accessed February 2015.
6. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial Hypercholesterolaemia is Underdiagnosed and Undertreated in the General Population: Guidance for Clinicians to Prevent Coronary Heart Disease. *Eur Heart J*. 2013;34:3478-3490.
7. Amgen Data on File, Investigator Brochure.
8. Abifadel M, Varret M, Rabes JP, et al. Mutations in PCSK9 Cause Autosomal Dominant Hypercholesterolemia. *Nat Genet*. 2003;34:154-156.

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