Amgen Presents Results Highlighting The Long-Term Safety And Efficacy Of Repatha® (Evolocumab) In The Longest Duration Study Of A PCSK9 Inhibitor To Date At AHA Scientific Sessions 2018

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Additional Data Analyzing Treatment Patterns in the United States Shows Underutilization of LDL-C Lowering Treatments in At-Risk Patients and Need for Improved Patient Awareness of Treatment Goals

THOUSAND OAKS, Calif., Nov. 12, 2018 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced the final report of the Open-Label Study of Long-TERm Evaluation Against LDL-C (OSLER-1), demonstrating long-term treatment with Repatha® (evolocumab) was associated with robust and consistent reductions in low-density lipoprotein cholesterol (LDL-C), with no increase in overall rates of adverse events over time and no neutralizing antibodies. Additionally, data from the Getting to an ImprOved Understanding of Low-Density Lipoprotein and Dyslipidemia Management (GOULD) Registry reflect a disconnect between physician perception of lipid-lowering therapies (LLTs) and their actual use, and highlight both a need for improved patient awareness of the goals of LLT and a need to address barriers to use of medications like Repatha.

In an effort to help more patients bring down the risk of heart attack and stroke, Amgen recently made Repatha available in the United States (U.S.) at a 60 percent reduced list price to address concerns over high out-of-pocket costs for patients. The results of all analyses were presented at the American Heart Association's Scientific Sessions 2018 in Chicago.

OSLER-1 is a five-year, open-label study evaluating the safety and efficacy of Repatha in hypercholesterolemia patients, including those with heterozygous familial hypercholesterolemia, on background statin therapy and patients with statin intolerance who were previously enrolled in one of five double-blind Repatha trials (N=1,324).[1-6] Patients treated with Repatha achieved a 59 percent reduction in mean LDL-C from baseline during the first year of treatment (n=785). With Repatha, the mean LDL-C reductions at years two, three, four and five were: 56 percent (n=1,071), 57 percent (n=1,001), 56 percent (n=943) and 56 percent (n=803), respectively. Adverse events (AE) were reported in 80 percent, 74 percent, 71 percent, 67 percent, and 65 percent of patients, respectively; serious AEs were reported in seven percent, seven percent, eight percent, seven percent, and seven percent of patients each year (years one through five, respectively).

"Amgen is pleased to present the results of OSLER-1, the longest study of a PCSK9 inhibitor to date, which clearly demonstrate the durable, long-term efficacy and safety of Repatha in reducing LDL-C levels," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "These findings are consistent with those observed in the Repatha cardiovascular outcomes study (FOURIER) and other Phase 3 trials, reinforcing Repatha's role in the treatment of high-risk patients who are unable to achieve sufficient LDL-C reduction through other means."

Analyses of data from GOULD, a multicenter, observational registry of people with atherosclerotic cardiovascular disease (ASCVD) designed to describe LDL-C treatment patterns in the U.S. over time (N= 5,006), demonstrated the underutilization of effective LLTs among patients at high-risk for cardiovascular events, in those with LDL-C levels ≥ 70 mg/dL. A survey of 110 physicians identified a disconnect between physicians' perceptions of LLTs and their actual use, with support for high-intensity statins and PCSK9 inhibition use at 75 percent among physicians and actual observed use of 50 percent and 10 percent, respectively. While many physicians had prescribed a PCSK9 inhibitor, those who had not, cited cost and hassle associated with prior authorization requirements from payers as important reasons for not prescribing.

Furthermore, among patients receiving any LLT, more than 70 percent did not know the main goal of this treatment was prevention of cardiovascular events and nearly half were unaware of their total lipid levels. GOULD data also demonstrated that, regardless of LLT type, a large proportion of patients remain unaware of their ASCVD risk, LDL-C levels, or therapy goals. This highlights an educational gap, which if addressed, may impact shared healthcare decision making and treatment adherence.

"Despite decades of research that has demonstrated the clear connection between lowering LDL-C levels and reducing the risk for cardiovascular events, several challenges, including cost and low awareness of this critical link have negatively impacted the use of PCSK9 inhibitors," said Murdo Gordon, executive vice president Global Commercial Operations at Amgen. "As demonstrated by our recent decision to make Repatha available in the U.S. at a 60 percent reduced list price, Amgen remains steadfast in its commitment to improving affordability for patients and supporting educational initiatives with the goal of advancing the effective management of LDL-C in high-risk patients to reduce cardiovascular risk."

OSLER-1 is part of Amgen's Program to Reduce LDL-C and cardiovascular Outcomes Following Inhibition of PCSK9 In different pOpulations (PROFICIO). PROFICIO is a large and comprehensive scientific research program evaluating Repatha in 32 clinical trials to date, with a combined enrollment of approximately 38,700 patients.[7]

OSLER-1 Study Design
Open Label Study of Long-TERm Evaluation Against LDL-C 1 (OSLER-1) is an open-label extension study with Repatha, a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor. The study was conducted across 192 sites in 18 countries.

Patients were eligible for participation in OSLER-1 provided that they did not discontinue treatment due to a treatment-related serious adverse event (SAE) during their qualifying Phase 2 study or require unblinded lipid measurements and/or adjustment of background lipid therapy during the first 12 weeks of OSLER-1. During the first year, patients were randomized 2:1 to Repatha 420 mg monthly in addition to standard of care (SOC) or SOC alone. After year one, all patients continuing in the study received Repatha 420 mg monthly in addition to SOC for the remaining 4 years of the study. Lipid parameters, safety and tolerability were assessed every 12 weeks.

The primary objective of the study is to evaluate the long-term safety and tolerability of Repatha. The secondary objective is to evaluate LDL-C reductions with Repatha over an extended period of time.

GOULD Study Design
Getting to an ImprOved Understanding of Low-Density Lipoprotein and Dyslipidemia Management (GOULD) Registry is a multicenter, observational

registry of ASCVD patients, to describe LDL-C treatment patterns in the United States and track them over time. This registry and subsequent analysis sought to better understand the adaptability of lipid management guidelines for patients with ASCVD.

From December 2016 to April 2018, interactive phone surveys with the lead physicians from each of the 120 U.S. centers participating in the registry (1 physician from each center) and patients (N=5,006) were conducted. Patients with ASCVD receiving any pharmacological LLT were eligible for enrollment in 1 of 3 cohorts: 1) currently receiving a PCSK9i antibody, 2) no PCSK9i and LDL-C 70-99 mg/dL, and 3) no PCSK9i and LDL-C ≥ 100 mg/dL. Patients underwent a 1-year retrospective chart review, followed by chart reviews and interviews every 6 months for 2 years.

About Repatha® (evolocumab)
Repatha 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.[8]

Repatha is approved in more than 60 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.

Important U.S. Product Information

Repatha is a PCSK9 (proprotein convertase subtilisin kexin type 9) inhibitor antibody indicated:

- to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease.
- as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia [HeFH]) to reduce low-density lipoprotein cholesterol (LDL-C).
- as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDLC.

The safety and effectiveness of Repatha have not been established in pediatric patients with HoFH who are younger than 13 years old or 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. Serious hypersensitivity reactions including angioedema have occurred in patients treated with Repatha.

Allergic reactions: Hypersensitivity reactions (e.g. angioedema, 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 patients treated with Repatha and occurring more frequently than placebo) were: nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site 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.

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%).

The most common adverse reactions in the Cardiovascular Outcomes Trial (>5% of patients treated with Repatha and occurring more frequently than placebo) were: diabetes mellitus (8.8% Repatha, 8.2% placebo), nasopharyngitis (7.8% Repatha, 7.4% placebo), and upper respiratory tract infection (5.1% Repatha, 4.8% placebo).

Among the 16,676 patients without diabetes mellitus at baseline, the incidence of new-onset diabetes mellitus during the trial was 8.1% in patients assigned to Repatha compared with 7.7% in those assigned to placebo.

Homozygous Familial Hypercholesterolemia (HoFH): The adverse reactions that occurred in at least two patients treated with Repatha and more frequently than placebo were: upper respiratory tract infection, influenza, gastroenteritis, and nasopharyngitis.

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 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.[9] 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 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 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. 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. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. 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. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

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