New Data Show Amgen's Repatha® (evolocumab) Significantly Reduced LDL-C And Non-HDL-C In High-risk Patients With Type 2 Diabetes

June 23, 2018

Data Presented at the 78th Scientific Sessions of the American Diabetes Association

THOUSAND OAKS, Calif., June 23, 2018 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced new data that show Repatha® (evolocumab) significantly reduced low-density lipoprotein cholesterol (LDL-C) and non-high density lipoprotein cholesterol (non-HDL-C) in patients with Type 2 diabetes and hypercholesterolemia or mixed dyslipidemia, taking the maximum tolerated dose of moderate/high-intensity statin therapy. BANTING was a dedicated study evaluating the efficacy of Repatha (monthly dosing), in lowering LDL-C and improving other lipid levels in patients with Type 2 diabetes.[1] In addition to meeting criteria for hypercholesterolemia or mixed dyslipidemia, patients in the trial had varying degrees of glycemic control. Data were presented at the American Diabetes Association 78th Annual Scientific Sessions.

"Diabetes affects more than 20 million Americans and managing their uncontrolled cholesterol levels remains a critical unmet need," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The findings of the BANTING study clearly demonstrate the ability for Repatha to help these patients reach their targets."

Results from the BANTING study show that in patients with Type 2 diabetes and hypercholesterolemia or mixed dyslipidemia (n=421), the addition of Repatha to background statin therapy resulted in significant reductions in LDL-C levels (53.1 percent and 64.1 percent mean reduction from baseline to week 12 and from baseline to the mean of weeks 10 and 12, respectively; $p<0.0001$).[1]

Type 2 diabetes is often associated with dyslipidemia, a condition characterized by low "good" cholesterol or HDL-C and elevated "bad" cholesterol or LDL-C.[2,3]

"Diabetes is one of the major controllable risk factors for cardiovascular disease, and many patients demonstrate poorly controlled LDL-C and non-HDL-C levels, despite treatment with statins," said Robert S. Rosenson, M.D., Icahn School of Medicine at Mount Sinai, and principal investigator of the BANTING study.* "These data are important, as they demonstrate that additional treatment options, such as Repatha, can help further reduce LDL-C and non-HDL-C in patients who are unable to reach targets with high-intensity statin therapy alone."

In addition to producing significant reductions in LDL-C levels, the addition of Repatha to background statin therapy enabled most patients to reach LDL-C levels recommended by current guidelines. The majority of patients in the Repatha group reached LDL-C levels of <70 mg/dL (84.5 percent versus 15.4 percent of patients in the placebo group at week 12 and 92.7 percent versus 14.8 percent of patients in the placebo group at the mean of weeks 10 and 12)[1] as recommended by the American College of Clinical Endocrinologists for patients with Type 2 diabetes and one or more risk factors.[4]

Treatment with Repatha was also associated with a significantly higher percentage of patients achieving the ≥50 percent reduction in LDL-C levels recommended by the American College of Cardiology (ACC) and the American Heart Association (AHA)[5] (65.5 percent versus 0.8 percent LDL-C reduction in Repatha versus patients in the placebo group at week 12 and 84.2 percent versus 0.7 percent LDL-C reduction in Repatha versus patients in the placebo group at the mean of weeks 10 and 12). Repatha also reduced several other lipid parameters, including non-HDL-C (47 percent versus 1 percent reduction with placebo at week 12, and 57 percent versus 1 percent reduction with placebo at the mean of weeks 10 and 12).[1] Non-HDL-C levels are a known risk factor for cardiovascular events in patients with Type 2 diabetes and together with LDL-C levels represent one of the primary targets of therapy recommended by guidelines.[6-8] These results are consistent with results from previous Phase 3 studies demonstrating Repatha's efficacy in reducing LDL-C and non-HDL-C levels in patients with Type 2 diabetes independent of glycemia, insulin use, renal function and cardiovascular disease status at baseline.[9]

The safety profile in BANTING was consistent with the established safety profile of Repatha.[9-11]

BANTING Study Design

The BANTING (evolocumaB efficAcy aNd safeTy IN type 2 diabetes mellitus on backGround statin therapy) study evaluated the effect of a 12 week regimen of monthly subcutaneous treatment with Repatha (420 mg dose) compared with placebo, on LDL-C and other lipid parameters in patients with Type 2 diabetes and hypercholesterolemia or mixed dyslipidemia while on optimized background statin therapy. The two co-primary endpoints were mean percent change in LDL-C from baseline to week 12 and to the mean of weeks 10 and 12. Secondary endpoints included proportion of patients who reached LDL levels <70 mg/dL, LDL-C reduction ≥50 percent and reduction in levels of other atherogenic lipids including non-HDL-C. The trial included patients 18 years of age or older with Type 2 diabetes, hemoglobin A1c <10 percent, who were receiving stable pharmacological therapy for diabetes for at least six months, and were taking a maximally tolerated dose of moderate or high intensity statin (per ACC/AHA definition). Eligibility criteria for LDL-C or non-HDL-C levels varied, depending on prior clinical cardiovascular disease. For more information about this trial, please visit www.clinicaltrials.gov under trial identification number NCT02739984.

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.[12]

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 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.

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 percent of Repatha-treated patients and occurring more frequently than placebo) in controlled trials involving patients with primary hyperlipidemia, including HeFH, 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 percent of Repatha-treated patients and 1 percent 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 percent versus 0 percent 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 percent and 3.0 percent 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 percent and 0 percent, respectively.

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

The safety profile of Repatha in the cardiovascular outcomes trial was generally consistent with the safety profile in the 12- and 52-week controlled trials involving patients with primary hyperlipidemia, including HeFH. Serious adverse events occurred in 24.8 percent and 24.7 percent of Repatha-treated and placebo-treated patients, respectively. Adverse events led to discontinuation of study treatment in 4.4 percent of patients assigned to Repatha and 4.2 percent assigned to placebo. Common adverse reactions (>5 percent of patients treated with Repatha and occurring more frequently than placebo) included diabetes mellitus (8.8 percent Repatha, 8.2 percent placebo), nasopharyngitis (7.8 percent Repatha, 7.4 percent placebo) and upper respiratory tract infection (5.1 percent Repatha, 4.8 percent placebo). Among the 16,676 patients without diabetes mellitus at baseline, the incidence of new-onset diabetes mellitus during the trial was 8.1 percent in patients assigned to Repatha compared with 7.7 percent in those assigned to placebo.

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 percent) Repatha-treated patients and more frequently than in placebo-treated patients, included upper respiratory tract infection (9.1 percent versus 6.3 percent), influenza (9.1 percent versus 0 percent), gastroenteritis (6.1 percent versus 0 percent), and nasopharyngitis (6.1 percent versus 0 percent).

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.[13] 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. 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. We or others could identify safety, side effects or manufacturing problems with our products, including our devices, after they are on the market. 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. Discovery or identification of new product candidates cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate will be successful and become a commercial product. 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.

*Dr. Robert Rosenson has received an honorarium from Amgen as a speaker.

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