New Analyses Presented At AHA 2017 Show Repatha® (evolocumab) Significantly Reduced Cardiovascular Events In Patients With Peripheral Artery Disease And In Patients With A History Of Heart Attacks

November 13, 2017

Data Support Use of Repatha to Reduce Risk of Recurrent Cardiovascular Events in Patients With History of Multiple Heart Attacks

Additional Analysis Found That Patients With More Recent Heart Attacks Experienced Substantial Risk Reductions With Repatha

Repatha Benefit in Peripheral Artery Disease Patients Presented at AHA Scientific Sessions 2017 and Simultaneously Published in "Circulation"

THOUSAND OAKS, Calif., Nov. 13, 2017 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced five new subgroup analyses from the Repatha® (evolocumab) cardiovascular outcomes study (FOURIER) that showed the addition of Repatha to statin therapy improved clinical outcomes with significant reduction of cardiovascular (CV) events, such as heart attack (also called myocardial infarction or MI) and stroke, in high-risk patients with peripheral artery disease (PAD), and in patients with a history of heart attack. The analyses, including two accepted for late-breaker scientific sessions, were presented at the American Heart Association (AHA) Scientific Sessions 2017.

"As we continue to look deeper into the data from the FOURIER study, we are able to identify subsets of patients that can derive even greater clinical benefit from intensive LDL-C lowering with evolocumab, in addition to what is achieved with statins alone," said Marc Sabatine, M.D., chairman, TIMI Study Group, Lewis Dexter, MD Distinguished Chair in Cardiovascular Medicine, Brigham and Women's Hospital and lead investigator of FOURIER. "These results offer additional ways for clinicians to tailor therapies for their patients to reduce the risk of recurrent cardiovascular events."

These results highlight Repatha's ability to reduce the residual risk for CV events particularly in high-risk patients with limited treatment options. One analysis showed the addition of Repatha to statin therapy improved clinical outcomes with significant reduction of CV events in patients with a history of PAD. Because of their greater baseline risk of CV events, there was a numerically greater absolute risk reduction (ARR) at 2.5 years in patients with PAD (ARR 4.1 percent, 95 percent CI 2.5-6.7) relative to those without PAD (ARR 1.5 percent, 95 percent CI 0.7-2.2). A separate analysis investigated the efficacy of Repatha in high-risk patients who have experienced a prior heart attack. In that analysis, the ARR was greater (~3 percent ARR over three years) in patients with a history of heart attack within two years compared to those whose heart attack was more than two years past (ARR 1 percent). Additionally, no new safety concerns were identified in these analyses.

"These analyses add to the growing body of evidence that Repatha significantly and consistently reduces cardiovascular event risk across a spectrum of high-risk cardiovascular patients," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The proven efficacy of Repatha to help those with established cardiovascular disease at high risk for heart attacks and strokes reinforces the importance of achieving and maintaining a low LDL-C level."

Repatha Significantly Reduces Risk of CV Events in Patients with PAD (Session LBS.02)
Of the 27,564 patients enrolled in the Repatha cardiovascular outcomes study, 3,642 of them had symptomatic PAD. Compared to those without PAD, these patients were older and had more CV risk factors including hypertension, smoking and diabetes. At 2.5 years, Repatha reduced the low-density lipoprotein cholesterol (LDL-C) levels in patients with PAD from a median of 93 to 31 mg/dL (p<0.001). In patients with PAD, Repatha significantly reduced the composite primary endpoint, which included hospitalization for unstable angina, coronary revascularization, heart attack, stroke or CV death, by 21 percent (2.5-year Kaplan-Meier rate 13.3 percent versus 16.8 percent, HR 0.79, 95 percent CI 0.66-0.94, p=0.0098) and the secondary composite endpoint of heart attack, stroke or CV death by 27 percent (9.5 percent versus 13.0 percent, HR 0.73, 95 percent CI 0.59-0.91, p=0.0040).

Repatha Demonstrated Significant Clinical Benefit Across a Range of High-Risk Patient Populations (Session LBS.02)
In a separate analysis, researchers evaluated the efficacy of Repatha in different MI subgroups. Patients with a history of MI (N=22,351) were characterized according to the time since their most recent MI event, number of previous MIs and presence of multivessel coronary artery disease (CAD). Treatment with Repatha resulted in a 24 percent relative risk reduction (RRR) (HR 0.76; 95 percent CI 0.64-0.89; p<0.001) in patients within two years of their most recent MI compared to 13 percent (HR 0.87; 95 percent CI 0.76-0.99; p=0.04) for those whose most recent MI occurred more than two years prior to enrollment. In those with multiple prior MIs, the RRR was 21 percent (HR 0.79; 95 percent CI 0.67-0.94; p=0.006) compared to 16 percent (HR 0.84; 95 percent CI 0.74-0.96; p=0.008) for those with only one previous MI, and patients with a history of multivessel CAD had a RRR of 30 percent (HR 0.70; 95 percent CI 0.58-0.84; p<0.001) compared to 11 percent RRR (HR 0.89; 95 percent CI 0.79-1.00; p=0.055) in patients without multivessel CAD.

Another analysis (Abstract #183) evaluating the totality of the primary endpoint events (both first and recurrent) during the course of the study revealed that treatment with Repatha improved clinical outcomes with significant reductions in total primary endpoint events driven by decreases in MI, stroke and coronary revascularization. Repatha reduced composite primary endpoint events by 18 percent (incidence-rate ratio 0.82, 95 percent CI 0.75-0.90, p<0.001).

The FOURIER trial recently showed that Repatha reduced major CV events compared to placebo in high-risk CV patients, including reducing MIs by 27 percent. Another new analysis (Abstract #184) revealed a robust benefit across the size and severity of MIs. Repatha was also effective in reducing the risk for MI regardless of size (significant reductions observed regardless of fold elevations in troponin levels) and severity (ST-elevation myocardial infarction/STEMI or non-STEMI). The Repatha benefit was highly significant and consistent regardless of MI size and reduced the risk of STEMI heart attack by 36 percent (HR 0.64; 95 percent CI 0.49-0.84; p<0.001).

Participants in the Repatha cardiovascular outcomes study were prospectively stratified according to their Thrombolysis in Myocardial Infarction (TIMI) Risk Score for Secondary Prevention to identify those with the greatest potential for clinical benefit following treatment with Repatha. Consistent with previous results, higher risk was associated with greater absolute risk reductions. (Abstract #3025)

Repatha Cardiovascular Outcomes (FOURIER) Study Design
FOURIER (Further Cardiovascular OUtcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk), a multinational Phase 3 randomized, double-blind, placebo-controlled trial, is designed to evaluate whether treatment with Repatha in combination with statin therapy compared to placebo plus statin therapy reduces cardiovascular events. The hard major adverse cardiovascular event (MACE) composite endpoint is the time to cardiovascular death, myocardial infarction or stroke (key secondary endpoint). The extended MACE composite endpoint is the time to cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization (primary endpoint).

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 1,300 study locations around the world were randomized to receive Repatha subcutaneous 140 mg every two weeks or 420 mg monthly plus effective statin dose; or placebo subcutaneous every two weeks or monthly plus effective 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 at least 1,630 patients experienced a key secondary endpoint.

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 percent 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 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).

Neurocognitive events were reported in less than or equal to 0.2 percent 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 percent of Repatha®-treated patients and 12.8 percent of placebo-treated patients. The most

common adverse reactions that occurred at a rate greater than placebo were back pain (3.2 percent versus 2.9 percent for Repatha® and placebo, respectively), arthralgia (2.3 percent versus 2.2 percent), and myalgia (2.0 percent versus 1.8 percent).

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.[2] 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.

CONTACT: Amgen, Thousand Oaks
Kristen Davis, 805-447-3008 (Media)
Kristen Neese, 805-313-8267 (Media)
Arvind Sood, 805-447-1060 (Investors)

References

1. Repatha® U.S. Prescribing Information. Amgen.
2. World Health Organization. Cardiovascular diseases (CVDs) fact sheet. http://www.who.int/mediacentre/factsheets/fs317/en/. Accessed October 30, 2017.

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