Landmark Outcomes Study Shows That Repatha® (Evolocumab) Decreases LDL-C To Unprecedented Low Levels And Reduces Risk Of Cardiovascular Events With No New Safety Issues

March 17, 2017

Repatha Significantly Reduces Risk of Hard Major Adverse Cardiovascular Events by 20 Percent

Risks of Heart Attack, Stroke and Coronary Revascularization Were Nominally Reduced by 27 Percent, 21 Percent and 22 Percent, Respectively

Patients in Study had History of Heart Attack, Stroke or Symptomatic Peripheral Arterial Disease and Were Treated With Optimized Statin Therapy

Amgen to Offer Innovative Refund Contracts in the U.S.

Detailed Results Simultaneously Published in the New England Journal of Medicine and Presented at the American College of Cardiology 66th Annual Scientific Session

THOUSAND OAKS, Calif., March 17, 2017 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the 27,564-patient Repatha® (evolocumab) cardiovascular outcomes study, FOURIER, established for the first time that maximally reducing low-density lipoprotein cholesterol (LDL-C) levels with Repatha, beyond what is possible with the current best therapy alone, leads to a further reduction in major cardiovascular events, including heart attacks, strokes and coronary revascularizations.

To view the multimedia assets associated with this release, please click: https://www.multivu.com/players/English/8004552-amgen-repatha-outcomes-study/

The study was statistically powered around the hard major adverse cardiovascular event (MACE) composite endpoint of first heart attack, stroke or cardiovascular death (key secondary composite endpoint) and found that adding Repatha to optimized statin therapy resulted in a statistically significant 20 percent (p<0.001) reduction in these events. The robust benefit in this objective measure started as early as six months and continued to accrue through the median 2.2 years of the study. In fact, the magnitude of the risk reduction in the hard MACE composite endpoint grew over time, from 16 percent in the first year to 25 percent beyond the first year.

The study also found a statistically significant 15 percent reduction (p<0.001) in the risk of the extended MACE composite (primary) endpoint, which included hospitalization for unstable angina, coronary revascularization, heart attack, stroke or cardiovascular death.

Patients on Repatha experienced a reduction in the risk of heart attack (27 percent, nominal p<0.001), stroke (21 percent, nominal p=0.01) and coronary revascularization (22 percent, nominal p<0.001). Consistent with recent trials of more intensive LDL lowering, there was no observed effect on cardiovascular mortality.[1-5] Similarly, there was no observed effect on hospitalization for unstable angina. In an exploratory analysis, the relative risk reduction for fatal and non-fatal heart attack or stroke was 19 percent in the first year (p=0.003) and 33 percent beyond the first year (p<0.00001).

"We now show for the first time in a dedicated outcomes study that decreasing LDL cholesterol with PCSK9 inhibition results in clinically meaningful cardiovascular benefit," said Marc S. Sabatine, M.D., M.P.H., chairman of the TIMI Study Group, the Lewis Dexter, MD, Distinguished Chair in Cardiovascular Medicine at Brigham and Women's Hospital, and Professor of Medicine, Harvard Medical School, Boston. "These benefits were achieved with lowering LDL cholesterol down to a median of 30 mg/dL, which is well below current targets, and the magnitude of risk reduction increased the longer patients were on therapy. These results support the need for long-term, vigorous LDL cholesterol reduction in our patients with cardiovascular disease."

When added to statin therapy, Repatha reduced LDL-C from a median of 92 to 30 mg/dL, a reduction of 59 percent at week 48, which was sustained throughout the trial. At 48 weeks, the LDL-C was reduced to at least 25 mg/dL in 42 percent of patients treated with Repatha, as compared with <0.1 percent in the placebo group (p<0.001). Additionally, treatment with Repatha had favorable effects on other lipid parameters.

"This is a game changer for high-risk patients. Even though these patients were optimally treated with the latest therapies, they were still at high risk for an additional cardiac event. It's remarkable to see such a large impact in reducing cardiac events given that this patient population was only on Repatha for about two years," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The absolute benefit will be even greater than what we observed in the Repatha outcomes trial, since the cardiovascular event rate in clinical practice is about 2-3 times higher than what is typically reported in a rigorously controlled outcomes trial."

Repatha was developed from the breakthrough work of Amgen scientists who elucidated the interaction of PCSK9 and the LDL receptor (LDLR), including the site where the LDLR binds to PCSK9, and developed antibodies that bind to PCSK9 at that site and block the interaction of PCSK9 with the LDLR. These scientific advances resulted in the intellectual property to antibodies to PCSK9 that protect Repatha. An extensive set of clinical trials subsequently demonstrated the effectiveness of Repatha in lowering LDL-C, in regressing coronary atherosclerosis and finally now in reducing the risk of major adverse cardiovascular events. From its inception, the program has demonstrated the power of human validation of a drug target based on genetic insights, an approach which is playing an increasingly important role across Amgen's therapeutic portfolio.

No new safety concerns were identified in this large clinical trial with roughly 60,000 patient-years of follow-up; this included the assessment of patients who achieved very low levels of LDL-C. In particular, there were no notable differences seen between treatment arms in the overall rate of adverse events, serious adverse events or adverse events leading to study drug discontinuation. Likewise, rates of adjudicated new onset diabetes (8.1 percent Repatha; 7.7 percent placebo), muscle-related side effects (5.0 percent Repatha; 4.8 percent placebo), cataract (1.7 percent Repatha; 1.8 percent placebo), neurocognitive adverse events (1.6 percent Repatha; 1.5 percent placebo) and allergic reactions (3.1 percent Repatha; 2.9 percent placebo) were similar between the two arms. Injection site reactions were more common with Repatha than with placebo (2.1 percent Repatha; 1.6 percent placebo). In the Repatha arm, post-baseline new binding antibodies were detected in 43 patients (0.3 percent) and neutralizing antibodies in none. Detailed results from the Repatha cognitive function study (EBBINGHAUS) will be presented in a separate Late-Breaking Clinical Trial Session on Saturday, March 18 at 9 a.m. ET.

Amgen to Offer Innovative Refund Contracts in the U.S.
To underscore the Company's conviction around these outcomes results, Amgen will offer additional contracting options in the U.S. to payers willing to remove access barriers. These options include one that offers a refund of the cost of Repatha for all of their eligible patients who have a heart attack or stroke. In addition, Amgen will continue to offer innovative contracts that provide reasonable budget predictability to help address budget impact concerns raised by payers.

"These robust data, from one of the largest outcomes trials ever conducted, validate that the net prices of Repatha in the market today are value-based. Now that Repatha has proven a meaningful reduction in cardiovascular events, we expect payers to remove onerous barriers and help appropriate patients get access to Repatha," said Joshua J. Ofman, M.D., MSHS, senior vice president of Global Value, Access and Policy at Amgen. "We look forward to working with payers to improve the health of their patients at high risk of heart attacks and strokes and discussing innovative contracting options over the coming months."

Amgen is committed to providing personalized support services for patients and providers in the U.S. through its Repatha*Ready* ™ program. Repatha*Ready* is a comprehensive suite of services to help patients and providers, including a Repatha co-pay card for eligible commercial patients, insurance coverage support and injection training. Amgen also provides patient assistance for its medicines marketed in the U.S. in a variety of ways, including free medicines through The Amgen Safety Net Foundation for qualifying individuals with no or limited drug coverage.

Webcast Information for Late-Breaking Clinical Trial Presentations
Live audio and video of the late-breaking clinical trial presentation will be broadcast over the internet simultaneously 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 at certain investor and medical conferences, can be accessed from 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.

Amgen Webcast Investor Meeting
Amgen will host a webcast investor meeting at ACC.17 at noon ET today. Sean E. Harper, M.D., executive vice president of Research and Development at Amgen, along with members of Amgen's clinical development team and clinical investigators, will participate at the investor meeting to discuss Amgen's cardiovascular program and data presented at ACC.17.

Live audio of the conference call will be broadcast over the internet simultaneously 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 at certain investor and medical conferences, can be found accessed 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.

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 primary endpoint is the time to cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization. The key secondary endpoint is the time to cardiovascular death, myocardial infarction or stroke.

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 1,200 study locations around the world were randomized to receive Repatha subcutaneous 140 mg every two weeks or 420 mg monthly plus optimized statin dose; or placebo subcutaneous every two weeks or monthly plus effective statin dose. Effective 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 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.[6]

Repatha is approved in more than 40 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% 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% of Repatha®-treated patients and 1% 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% versus 0% 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% and 3.0% 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% and 0%, respectively.

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%).

Neurocognitive events were reported in less than or equal to 0.2% 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% of Repatha® -treated patients and 12.8% of placebo-treated patients. The most common adverse reactions that occurred at a rate greater than placebo were back pain (3.2% versus 2.9% for Repatha® and placebo, respectively), arthralgia (2.3% versus 2.2%), and myalgia (2.0% versus 1.8%).

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

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.[7] 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 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 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 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. 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.

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Repatha® (evolocumab) Product Shot

Repatha Cardiovascular Outcomes (FOURIER) Study Design Fact Sheet

Repatha® (evolocumab) Fact Sheet

Repatha® (evolocumab) Logo



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