FDA Approves Amgen's Repatha® (evolocumab) To Prevent Heart Attack And Stroke

December 1, 2017

Following FDA Priority Review, Repatha is the Only PCSK9 Inhibitor Approved to Reduce Risk of Heart Attack, Stroke and Coronary Revascularization

THOUSAND OAKS, Calif., Dec. 1, 2017 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that following priority review of its supplemental Biologics License Application, the U.S. Food and Drug Administration (FDA) approved Repatha® (evolocumab) as the first PCSK9 inhibitor to prevent heart attacks, strokes and coronary revascularizations in adults with established cardiovascular disease.[1]

"We are pleased that the FDA made the inclusion of our outcomes data a priority so that patients can benefit from Repatha's ability to reduce life-changing events of heart attacks and strokes," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Despite treatment with current best therapy, many patients are still at high risk for cardiovascular events. Physicians now have a new FDA-approved treatment option to prevent cardiovascular events by dramatically lowering LDL cholesterol with Repatha, especially for patients already on maximally-tolerated statin therapy who need further LDL cholesterol lowering."

In the Repatha cardiovascular outcomes study (FOURIER), Repatha reduced the risk of heart attack by 27 percent, the risk of stroke by 21 percent and the risk of coronary revascularization by 22 percent.[2]

"In the U.S., every 40 seconds someone has a heart attack or stroke, and nearly one in three of these patients will have another event, leading to a societal cost that exceeds $600 billion annually. With this approval, it's now more important than ever that appropriate patients obtain access to Repatha in order to avoid preventable heart attacks and strokes. We will continue to work with payers to help ensure the patients who need Repatha the most are able to get this innovative medicine," said Anthony C. Hooper, executive vice president of Global Commercial Operations at Amgen.

The FDA also approved Repatha to be used as an adjunct to diet, alone or in combination with other lipid-lowering therapies, such as statins, for the treatment of adults with primary hyperlipidemia to reduce low density lipoprotein cholesterol (LDL-C).[1]

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 $5 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.

Repatha Cardiovascular Outcomes (FOURIER) Study: Key Outcomes

The 27,564-patient Repatha cardiovascular outcomes study (FOURIER) demonstrated that adding Repatha to optimized statin therapy resulted in a statistically significant 20 percent (p<0.001) reduction in major adverse cardiovascular events (MACE) represented in the key secondary composite endpoint of time to first heart attack, stroke or cardiovascular death. The study found a statistically significant 15 percent reduction (p<0.001) in the risk of the primary composite endpoint, which included hospitalization for unstable angina, coronary revascularization, heart attack, stroke or cardiovascular death.

The magnitude of risk reduction in both the primary and key secondary composite endpoints grew over time, with the robust benefit starting as early as six months and accruing through the median 2.2 years of the study.

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).[2] Consistent with recent trials of more intensive LDL-C lowering, there was no observed effect on cardiovascular mortality. Similarly, there was no observed effect on hospitalization for unstable angina.[3-7]

The safety profile of Repatha in the outcomes trial was generally consistent with the safety profile for the 12- and 52-week controlled trials involving patients with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH). Common adverse reactions included diabetes mellitus, nasopharyngitis, and upper respiratory tract infection.

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 high- or moderate-intensity statin therapy compared to placebo plus statin therapy reduces cardiovascular events. The hard 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 established 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 high- or moderate-intensity effective statin dose; or placebo subcutaneous every two weeks or monthly plus high- to moderate-intensity statin dose. Statin therapy was defined in the protocol 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 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 LDL-C.

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 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.[8] 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.

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

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