European Commission Approves Amgen's New Cholesterol-Lowering Medication Repatha™ (evolocumab), The First PCSK9 Inhibitor To Be Approved In The World, For Treatment Of High Cholesterol

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Critical Milestone for Patients With Uncontrolled Cholesterol who Require Additional Intensive LDL-C Reduction

THOUSAND OAKS, Calif., July 21, 2015 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the European Commission (EC) has granted marketing authorization for Repatha ™(evolocumab), the first proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor to be approved in the world, for the treatment of patients with uncontrolled cholesterol who require additional intensive low-density lipoprotein cholesterol (LDL-C) reduction. Repatha is a human monoclonal antibody that inhibits PCSK9, a protein that reduces the liver's ability to remove LDL-C, or "bad" cholesterol, from the blood.[1] Elevated LDL-C is an abnormality of cholesterol and/or fats in the blood,[2,3] and is recognized as a major risk factor for cardiovascular disease (CVD).[4,5]

To view the multimedia assets associated with this press release, please click: http://www.multivu.com/players/English/7414052-amgen-repatha/.

The EC approved Repatha for:

- The treatment of adults with primary hypercholesterolemia (heterozygous familial and non-familial [HeFH]) or mixed dyslipidemia, as an adjunct to diet:
  - in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin, or
  - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.
- The treatment of adults and adolescents aged 12 years and over with homozygous familial hypercholesterolemia (HoFH) in combination with other lipid-lowering therapies.

The effect of Repatha on cardiovascular morbidity and mortality has not yet been determined.

More than 60 percent of high-risk patients in Europe are still unable to adequately lower their LDL-C levels with statins or other currently approved lipid-lowering agents. Among very high-risk patients, the percentage is increased to more than 80 percent.[6] The health care cost of CVD in the European Union (EU) is approximately €106 billion per year.[7]

"We are proud that our cholesterol-lowering medication, Repatha, is the first PCSK9 inhibitor to be approved by any regulatory agency in the world," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "High LDL cholesterol is a major global health burden and many patients are unable to appropriately control their LDL cholesterol with the maximum tolerated dose of a statin, or are unable to take statins due to intolerance or contraindications. We are excited to make this new cholesterol-lowering medication available for patients in Europe."

One high-risk patient group includes those with familial hypercholesterolemia (FH), an inherited condition caused by genetic mutations which lead to high levels of LDL-C at an early age.[8] It is estimated that less than one percent of people with FH (heterozygous and homozygous forms) in most countries are diagnosed.[9]

"Many patients who are taking cholesterol-lowering therapies, including those with familial hypercholesterolemia, still struggle to control their LDL cholesterol levels," said John J.P. Kastelein, professor of medicine and chairman of the Department of Vascular Medicine at the Academic Medical Center (AMC) of the University of Amsterdam. "As the first in a new class of drugs in the European Union, evolocumab will offer physicians an important and innovative treatment option for patients with uncontrolled cholesterol who require additional LDL cholesterol reduction."

Approval from the EC grants a centralized marketing authorization with unified labeling in the 28 countries that are members of the EU. Norway, Iceland and Liechtenstein, as members of the European Economic Area (EEA), will take corresponding decisions on the basis of the decision of the EC.

Data show Repatha has demonstrated substantial and consistent reductions in LDL-C levels with supporting beneficial changes in other lipid parameters in approximately 6,000 patients with primary hyperlipidemia and mixed dyslipidemia, including more than 4,500 patients with high cholesterol in 10 Phase 3 trials.[10] In these studies, Repatha significantly reduced LDL-C by approximately 55 percent to 75 percent compared with placebo,[11-14] and by approximately 35 percent to 45 percent compared with ezetimibe.[11,12,14] In patients with homozygous FH, Repatha significantly reduced LDL-C by approximately 15 percent to 30 percent compared with placebo.[15] Reduction of LDL-C was maintained with long-term treatment.[16]

The adverse event profile for Repatha was comparable overall to that of the control groups.[11-17] The most common adverse reactions that occurred in greater than or equal to 2 percent of the Repatha group, and more frequently than in the control group, were nasopharyngitis, upper respiratory tract infection, back pain, arthralgia, influenza and nausea. Please consult the Summary of Product Characteristics (SmPC) for full safety information.

Repatha is for subcutaneous injection into the abdomen, thigh or upper arm region. Injection sites should be rotated and injections should not be given into areas where the skin is tender, bruised, red or hard. Repatha must not be administered intravenously or intramuscularly. Before starting treatment with Repatha, secondary causes (non-genetic) of excess cholesterol and abnormal fat levels in blood should be excluded. The medicine can only be obtained with a prescription.

The recommended dose for adults with primary disease is either 140 mg every two weeks or 420 mg (the contents of three pre-filled syringes) once a month; both doses are clinically equivalent. For adults or children older than 12 years with homozygous FH, the initial recommended dose is 420 mg once a month. If a response is not achieved after 12 weeks of treatment, the dose can be increased up to 420 mg every two weeks. For more information, see the package leaflet.

About Repatha™ (evolocumab)

Repatha ™(evolocumab) is a human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9).[1] PCSK9 is a protein that targets LDL receptors for degradation and thereby reduces the liver's ability to remove LDL-C, or "bad" cholesterol, from the blood.[18] Repatha, developed by Amgen scientists, is designed to bind to PCSK9 and inhibit PCSK9 from binding to LDL receptors on the liver surface. In the absence of PCSK9, there are more LDL receptors on the surface of the liver to remove LDL-C from the blood.[1]

Important EU Product Information

Hypercholesterolemia and mixed dyslipidemia

Repatha is indicated in adults with primary hypercholesterolemia (heterozygous familial and non-familial) or mixed dyslipidemia, as an adjunct to diet:

- in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

Homozygous familial hypercholesterolemia

Repatha is indicated in adults and adolescents aged 12 years and over with homozygous familial hypercholesterolemia in combination with other lipid-lowering therapies.

The effect of Repatha on cardiovascular morbidity and mortality has not yet been determined.

Important Safety Information

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Special Warnings and Precautions: Renal impairment: Patients with severe renal impairment (defined as eGFR < 30 mL/min/1.73 m^2) have not been studied. Repatha should be used with caution in patients with severe renal impairment. Hepatic impairment: In patients with moderate hepatic impairment, a reduction in total evolocumab exposure was observed that may lead to a reduced effect on LDL-C reduction. Therefore, close monitoring may be warranted in these patients. Patients with severe hepatic impairment (Child-Pugh C) have not been studied. Repatha should be used with caution in patients with severe hepatic impairment. Dry natural rubber: The needle cover of the glass pre-filled syringe and of the pre-filled pen is made from dry natural rubber (a derivative of latex), which may cause allergic reactions. Sodium content: Repatha contains less than 1 mmol sodium (23 mg) per dose, i.e. it is essentially 'sodium-free'.

Interactions: No formal drug-drug interaction studies have been conducted for Repatha. No studies on pharmacokinetic and pharmacodynamics interaction between Repatha and lipid-lowering drugs other than statins and ezetimibe have been conducted.

Fertility, Pregnancy and Lactation: There are no or limited amount of data from the use of Repatha in pregnant women. Repatha should not be used during pregnancy unless the clinical condition of the woman requires treatment with evolocumab. It is unknown whether evolocumab is excreted in human milk. A risk to breastfed newborns/infants cannot be excluded. No data on the effect of evolocumab on human fertility are available.

Undesirable Effects: The following common (≥ 1/100 to < 1/10) adverse reactions have been reported in pivotal, controlled clinical studies: influenza, nasopharyngitis, upper respiratory tract infection, rash, nausea, back pain, arthralgia, injection site reactions. Please consult the SmPC for a full description of undesirable effects.

Pharmaceutical Precautions: Store in a refrigerator (2 degrees C – 8 degrees C). Do not freeze. Keep the pre-filled syringe or the pre-filled pen in the original carton in order to protect from light. If removed from the refrigerator, Repatha may be stored at room temperature (up to 25 degrees C) in the original carton and must be used within 1 week.

About Amgen Cardiovascular

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.[19] 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 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 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 management's current expectations and beliefs and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. 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 (SEC) reports filed by Amgen, including Amgen's most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen's most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Amgen is providing this information as of July 21, 2015, and expressly disclaims any duty to update information contained in this news release.

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. 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 after they are on the market. Our business may be impacted by government investigations, litigation and products liability claims. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products are affected by the reimbursement policies imposed by third-party payors, 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 as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of our products. In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, 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 and there can be no guarantee of our ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, 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 integrate the operations of companies we have acquired may not be successful. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plan. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or their ability to pay a dividend or repurchase our common stock.

The scientific information discussed in this news release related to our product candidates is specific to the European Union. Such product candidates are not approved by the U.S. Food and Drug Administration (FDA), and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates in the U.S.

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