Journal Of The American Medical Association Publishes Phase 3 LAPLACE-2 Study Showing Evolocumab Significantly Reduced LDL Cholesterol In Patients On Statins Regardless Of Statin Dose

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THOUSAND OAKS, Calif., May 13, 2014 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced the publication of data from the Phase 3 LAPLACE-2 (LDL-C Assessment with PCSK9 MonoclonaL Antibody Inhibition Combined with Statin ThErapy-2) study in the *Journal of the American Medical Association (JAMA).* Results from the 12-week study, which evaluated 1,896 patients with high cholesterol, showed treatment with subcutaneous evolocumab (140 mg every two weeks or 420 mg monthly) in combination with different daily doses of statin therapy significantly reduced mean low-density lipoprotein cholesterol (LDL-C) regardless of statin dose. These findings were initially presented at the American College of Cardiology's 63rd Annual Scientific Session (ACC.14) in March 2014.

Evolocumab, an investigational fully human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9), a protein that reduces the liver's ability to remove LDL-C from the blood[1], reduced mean LDL-C by 55-76 percent from baseline compared to placebo and 38-47 percent from baseline compared to ezetimibe (p<0.001). No adverse events (AEs) occurred in ≥ 2 percent of the evolocumab combined group. The most common AEs in the evolocumab combined group were back pain, arthralgia, headache, muscle spasms and pain in extremity.

"Elevated LDL cholesterol is recognized as a major risk factor for cardiovascular disease, and although statins are effective in reducing LDL cholesterol levels, many patients may need additional LDL cholesterol lowering," said lead investigator Jennifer G. Robinson, M.D., M.P.H., director of the Prevention Intervention Center, professor of the Departments of Epidemiology & Medicine, College of Public Health at the University of Iowa. "This is the first study to demonstrate that the addition of evolocumab results in similar percent reductions in LDL cholesterol and achieved LDL cholesterol levels regardless of stable baseline statin type, dose or intensity, across three commonly prescribed statins and a broad range of doses."

There are approximately 300 million cases of dyslipidemia in the U.S., Japan and Western Europe.[2] According to the Centers for Disease Control and Prevention, more than 71 million American adults have high LDL-C[3], or "bad" cholesterol, and elevated LDL-C is recognized as a major risk factor for cardiovascular disease.[4,5]

"Results from the Phase 3 LAPLACE-2 study show that evolocumab provided cholesterol-lowering regardless of statin therapy and we look forward to bringing this new treatment option to patients who are taking statins and still need additional treatment options to lower their cholesterol levels," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "These results in combination with data from other studies in our clinical trial program form the basis of our global filing plan for evolocumab and we are working closely with regulatory authorities to provide this treatment to patients with high cholesterol."

LAPLACE-2 Study Design

LAPLACE-2 (LDL-C Assessment with PCSK9 MonoclonaL Antibody Inhibition Combined with Statin ThErapy-2) is a Phase 3 randomized, multicenter, double-blind, placebo- and ezetimibe-controlled study designed to evaluate safety, tolerability and efficacy of evolocumab in 1,896 patients with primary hypercholesterolemia and mixed dyslipidemia (LDL-C ≥80 mg/dL) when added to statin therapy. Patients were randomized to one of 24 treatment groups in a two-step randomization. Eligible patients were initially randomized to one of five open label background statin treatments: atorvastatin 10 mg, atorvastatin 80 mg, rosuvastatin 5 mg, rosuvastatin 40 mg or simvastatin 40 mg daily. Patients randomized to atorvastatin were then randomized to one of six treatment groups: evolocumab every two weeks and oral placebo, evolocumab every month and oral placebo, subcutaneous placebo every two weeks and oral placebo, subcutaneous placebo every month and oral placebo, subcutaneous placebo every two weeks and ezetimibe 10 mg, or subcutaneous placebo every month and ezetimibe 10 mg. Patients randomized to rosuvastatin or simvastatin were then randomized to one of four treatment groups: evolocumab every two weeks, evolocumab every month, subcutaneous placebo every two weeks, or subcutaneous placebo every month.

The co-primary endpoints were the mean percent change from baseline in LDL-C at weeks 10 and 12 and the percent change in LDL-C reduction at week 12. Co-secondary efficacy endpoints included means at weeks 10 and 12 and at week 12 for the following: LDL-C <70 mg/dL; absolute change from baseline in LDL-C; and the percentage change from baseline in non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (ApoB), total cholesterol (TC)/HDL-C ratio, ApoB/apolipoprotein A1 (ApoA1) ratio, lipoprotein(a), triglycerides, HDL-C and very low-density lipoprotein cholesterol (VLDL-C).

About Evolocumab

Evolocumab is a fully 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.[6] Evolocumab, being 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]

About PROFICIO: The Evolocumab Clinical Trial Program

PROFICIO, which stands for the Program to Reduce LDL-C and Cardiovascular Outcomes Following Inhibition of PCSK9 In Different POpulations, is a large and comprehensive clinical trial program evaluating evolocumab in 20 clinical trials, with a combined planned enrollment of nearly 30,000 patients.

The Phase 3 program includes 14 trials to evaluate evolocumab administered every two weeks and monthly in multiple patient populations, including in combination with statins in patients with hyperlipidemia (LAPLACE-2 and YUKAWA-2); in patients with hyperlipidemia who cannot tolerate statins (GAUSS-2 and GAUSS-3); as a stand-alone treatment in patients with hyperlipidemia (MENDEL-2); in patients whose elevated cholesterol is caused by genetic disorders called heterozygous (RUTHERFORD-2 and TAUSSIG) and homozygous (TESLA and TAUSSIG) familial hypercholesterolemia; as well as the administration of evolocumab (THOMAS-1 and THOMAS-2).

Five studies in the evolocumab Phase 3 program will provide long-term safety and efficacy data. These include FOURIER (Further Cardiovascular OUtcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk), which will assess whether treatment with evolocumab in combination with statin therapy compared to placebo and statin therapy reduces recurrent cardiovascular events in approximately 22,500 patients with cardiovascular disease; DESCARTES (Durable Effect of PCSK9 Antibody CompARed wiTh PlacEbo Study) in patients with hyperlipidemia at risk for cardiovascular disease; OSLER-2 (Open Label Study of Long TERm Evaluation Against LDL-C Trial-2) in patients with high cholesterol who completed any of the Phase 3 studies; GLAGOV (GLobal Assessment of Plaque ReGression with a PCSK9 AntibOdy as Measured by IntraVascular Ultrasound), which will determine the effect of evolocumab on coronary atherosclerosis in approximately 950 patients undergoing cardiac catheterization; and TAUSSIG (Trial Assessing Long Term USe of PCSK9 Inhibition in Subjects with Genetic LDL Disorders), which will assess the long-term safety and efficacy of evolocumab on LDL-C in patients with severe familial hypercholesterolemia.

About Amgen's Commitment to Cardiovascular Disease
Amgen is dedicated to addressing important scientific questions in order to advance care and improve the lives of patients with cardiovascular disease. Through its own research and development efforts and innovative partnerships, Amgen has built a robust cardiology pipeline consisting of several 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 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 May 13, 2014, 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 Amgen Inc. and its subsidiaries (which are collectively referred to as we, or us) 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 and our partners 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 product liability claims. 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. 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 (including products of our wholly-owned subsidiaries) are affected by the 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 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 and our partners routinely obtain patents for products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by our competitors and there can be no guarantee of our or our partners' 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.

The scientific information discussed in this news release related to our product candidates is preliminary and investigative. 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.

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