The Lancet Publishes Two Phase 3 Studies Showing Cholesterol-Lowering Medication Evolocumab Significantly Reduced LDL Cholesterol In Patients With Serious Genetic Disorders That Cause High Cholesterol

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Data From Phase 3 RUTHERFORD-2 Study Show Evolocumab Significantly Reduced Mean LDL-C by 59-66 Percent Compared to Placebo in Patients With Heterozygous Familial Hypercholesterolemia

Phase 3 TESLA Data Show Evolocumab Significantly Reduced LDL-C by 31 Percent Compared to Placebo in Patients With Homozygous Familial Hypercholesterolemia

THOUSAND OAKS, Calif., Oct. 1, 2014 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced *The Lancet* published data from two Phase 3 studies, RUTHERFORD-2 and TESLA, that showed treatment with evolocumab, a novel investigational low-density lipoprotein cholesterol (LDL-C)-lowering medication, resulted in a statistically significant reduction in LDL-C compared to placebo in patients with different types of familial hypercholesterolemia (FH).[1,2] Familial hypercholesterolemia is an inherited condition caused by a gene mutation which leads to high levels of LDL-C, or "bad" cholesterol, and premature cardiovascular disease.[3]

Evolocumab is 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.[4]

The RUTHERFORD-2 study evaluating 329 patients with heterozygous FH (HeFH) showed that adding subcutaneous evolocumab (140 mg every two weeks or 420 mg monthly) to a stable dose of statin and other lipid-lowering therapies significantly reduced mean LDL-C by 59-66 percent from baseline compared to placebo at week 12 and weeks 10 and 12 (p<0.001). At week 12, an LDL-C level of 70 mg/dL (1.8 mmol/L) was achieved by 68 percent of patients treated with evolocumab 140 mg every two weeks and by 63 percent of patients treated with evolocumab 420 mg monthly, versus 2 percent of patients in the placebo groups (p<0.0001 each). Similar results were seen for the mean of weeks 10 and 12 (both doses p<0.0001). The most common adverse events (AEs) reported in the publication in evolocumab-treated patients were nasopharyngitis, headache, contusion (i.e., bruise), back pain and nausea. Results from the RUTHERFORD-2 study were initially presented at the American College of Cardiology's 63rd Annual Scientific Session (ACC.14) in March 2014.

"Statin therapy has led to significant improvements in the treatment of familial hypercholesterolemia, however many patients are still not able to achieve desirable LDL cholesterol levels despite intensive treatment," said lead investigator Frederick J. Raal, M.D., University of Witwatersrand, Johannesburg, South Africa. "Results from the RUTHERFORD-2 and TESLA studies show that evolocumab offers the potential to achieve significant further reductions in LDL cholesterol in these difficult-to-treat and high-risk populations."

The TESLA study evaluating 49 patients with homozygous FH (HoFH), not on apheresis, showed that adding evolocumab 420 mg subcutaneous monthly to a stable dose of statin therapy and other lipid-lowering medications significantly reduced LDL-C by 31 percent (95 percent CI, -44, -18, p<0.001) from baseline at week 12 compared to placebo. In patients with at least one defective LDL receptor mutation, evolocumab reduced LDL-C by 41 percent (95 percent CI, -53, -28, p<0.0001) compared to placebo. The most common AEs (more than one subject) in evolocumab-treated patients were upper respiratory tract infection, influenza, gastroenteritis and nasopharyngitis. Results from the TESLA study were initially presented at the 82nd Congress of the European Atherosclerosis Society (EAS 2014) in June 2014.

"Results from these two Phase 3 studies support the effectiveness of evolocumab as a treatment option for patients with both forms of familial hypercholesterolemia, who struggle to manage 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 a number of other studies in our clinical trial program, formed the basis of our U.S. and EU filing submissions for evolocumab and we are working with regulatory authorities to bring this important treatment option to patients with significant unmet medical need."

High cholesterol, particularly elevated LDL-C, is the most common form of dyslipidemia, which is an abnormality of cholesterol and/or fats in the blood.[5,6] Elevated LDL-C is recognized as a major risk factor for cardiovascular disease.[7,8] Familial hypercholesterolemia is an inherited condition caused by genetic mutations which lead to high levels of LDL-C at an early age,[3] and it is estimated that less than one percent of people with FH (heterozygous and homozygous forms) in the U.S. are diagnosed.[9]

Patients can have either one of two types of FH.[3] Heterozygous FH is the more common type of FH and occurs globally in approximately one in 200 to 500 people.[9] It can cause LDL-C levels twice as high as normal (e.g., >190 mg/dL).[10] Individuals with HeFH have one altered copy of a cholesterol-regulating gene.[10] Homozygous FH is the rare, more severe form, occurring in approximately one in a million individuals.[11] It can cause LDL-C levels more than six times as high as normal (e.g., 650-1,000 mg/dL).[11] An individual with HoFH has two altered copies of cholesterol-regulating genes (one from each parent).[3] In 2013, the U.S. Food and Drug Administration (FDA) granted evolocumab an orphan drug designation for HoFH.

RUTHERFORD-2 Study Design

RUTHERFORD-2 (RedUction of LDL-C with PCSK9 InhibiTion in HEteRozygous Familial HypercholesteRolemia Disorder Study-2) is a Phase 3 randomized, multicenter, double-blind, placebo-controlled trial designed to evaluate the safety, tolerability and efficacy of evolocumab in 329 patients with HeFH and an LDL-C ≥100 mg/dL who were on a stable dose of statin therapy and lipid-lowering medication. Patients were randomized to one of four treatment groups to compare subcutaneous evolocumab (140 mg every two weeks or 420 mg monthly) with subcutaneous placebo (every two weeks or monthly). The co-primary endpoints were the percent reduction from baseline in LDL-C at week 12 and the mean percent reduction from baseline in LDL-C at weeks 10 and 12. Co-secondary efficacy endpoints included means at weeks 10 and 12 and at week 12 for the following: absolute change from baseline in LDL-C; LDL-C <70 mg/dL; 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).

TESLA Study Design
TESLA (Trial Evaluating PCSK9 Antibody in Subjects with LDL Receptor Abnormalities) is a two-part Phase 2/3 trial designed to evaluate the safety, tolerability and efficacy of evolocumab.

The Phase 3 12-week, double-blind, randomized, placebo-controlled, multicenter part of the TESLA trial (TESLA Part B) evaluated evolocumab compared to placebo in 49 adults and adolescents aged 12 years and over with HoFH (LDL-C ≥130 mg/dL) who were on a stable dose of statin therapy and other lipid-lowering medications and were not receiving apheresis. Patients were randomized to evolocumab 420 mg subcutaneous monthly or placebo subcutaneous monthly. The primary endpoint was the percent reduction from baseline in LDL-C at week 12. Secondary endpoints included mean percent change from baseline in LDL-C, apolipoprotein B (ApoB) and lipoprotein(a) (Lp(a)) at weeks 6 and 12, and percent change from baseline in ApoB and Lp(a) at week 12.

The Phase 2 12-week, open-label, single-arm, multicenter part of the TESLA trial (TESLA Part A) evaluated eight patients with HoFH who were on stable drug therapy for four weeks or more. Patients received evolocumab 420 mg subcutaneous once monthly for 12 weeks. The primary endpoint was the percent reduction from baseline in LDL-C at week 12. Positive results from the Phase 2 TESLA trial were presented at the 81st Congress of the European Atherosclerosis Society (EAS 2013) and published in Circulation.[12]

About Evolocumab
Evolocumab is a fully human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9).[4] 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.[13] 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.[4]

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 22 clinical trials, with a combined planned enrollment of approximately 30,000 patients.

The Phase 3 program includes 16 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; the effects of evolocumab on lipoprotein metabolism (FLOREY); and the administration of evolocumab in statin-treated hyperlipidemic patients (THOMAS-1 and THOMAS-2).

Five ongoing 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; EBBINGHAUS (Evaluating PCSK9 Binding AntiBody Influence oN CoGnitive HeAlth in High CardiovascUlar Risk Subjects), which will evaluate the effect of evolocumab on cognitive function in a subset of patients enrolled in FOURIER; 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 including patients with homozygous familial hypercholesterolemia. The DESCARTES (Durable Effect of PCSK9 Antibody CompARed wiTh PlacEbo Study) study, a long-term safety and efficacy trial in patients with hyperlipidemia at risk for cardiovascular disease, has been completed, presented and published.

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 Oct. 1, 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 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. Cost saving initiatives may result in us incurring impairment or other related charges on our assets. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plans. 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 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.

CONTACT: Amgen
Kristen Davis: 805-447-3008 (media)
Arvind Sood: 805-447-1060 (investors)

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