Amgen Announces Positive Top-Line Results From Phase 3 RUTHERFORD-2 Trial Of Evolocumab (AMG 145) In Patients With Heterozygous Familial Hypercholesterolemia

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RUTHERFORD-2 Study Meets Co-Primary Endpoints of LDL Cholesterol Reduction
Amgen Also Announces Results From Phase 3 Study With Automated Mini-Doser
Completion of Fifth Phase 3 Study Forms Basis For Global Filing Plan

THOUSAND OAKS, Calif., Jan. 30, 2014 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the Phase 3 RUTHERFORD-2 (RedUction of LDL-C with PCSK9 InhibiTion in HEteRozygous Familial HypercholesteRolemia Disorder Study-2) trial evaluating evolocumab in combination with statins and other lipid-lowering therapies in patients with heterozygous familial hypercholesterolemia (HeFH) met its co-primary endpoints: the percent reduction from baseline in low-density lipoprotein cholesterol (LDL-C) at week 12 and the mean percent reduction from baseline in LDL-C at weeks 10 and 12. The mean percent reductions in LDL-C, or "bad" cholesterol, were consistent with the results observed for the same doses in the Phase 2 RUTHERFORD trial for evolocumab compared to placebo.[1]

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.[2]

The RUTHERFORD-2 trial evaluated safety, tolerability and efficacy of evolocumab in 329 HeFH patients on a stable dose of statin and other lipid-lowering therapies. 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).

Safety was balanced across treatment groups except for the following most common adverse events (≥ 2 percent in evolocumab combined group and ≥ 2 percent compared to placebo): nasopharyngitis (8.6 percent evolocumab; 4.6 percent placebo), contusion (4.1 percent evolocumab; 0.9 percent placebo), back pain (3.6 percent evolocumab; 0.9 percent placebo), nausea (3.6 percent evolocumab; 0.9 percent placebo), influenza (3.2 percent evolocumab; 0.0 percent placebo), and myalgia (2.7 percent evolocumab; 0.0 percent placebo).

"Data from the RUTHERFORD-2 study suggest that evolocumab, when used as an add-on therapy to existing lipid-lowering medications, may offer a new treatment option for patients with heterozygous familial hypercholesterolemia," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "The RUTHERFORD-2 study is the fifth pivotal LDL-C lowering study in our Phase 3 program. The robust data from these five studies will form the basis of our global filing plan and we look forward to discussions with regulatory agencies."

Details of the Phase 3 RUTHERFORD-2 study results will be submitted to a future medical conference and for publication.

In a separate Phase 3 study that enrolled 164 patients with high cholesterol on statin therapy, 95 percent or greater of patients were able to self-administer at least one full home administration of evolocumab 420 mg subcutaneously by one injection with an automated mini-doser or by three injections with a standard spring-based autoinjector. Reductions in LDL-C were comparable with both devices and consistent to those seen in the Phase 2 LAPLACE-TIMI 57 (LDL-C Assessment with PCSK9 MonoclonaL Antibody Inhibition Combined with Statin ThErapy -Thrombolysis In Myocardial Infarction-57) trial. Safety was balanced between the treatment groups and no new safety concerns were identified.

According to the Centers for Disease Control and Prevention, more than 71 million American adults have high LDL-C.[3] Elevated LDL-C is recognized as a major risk factor for cardiovascular disease.[4-5] Patients with familial hypercholesterolemia, an inherited condition that causes high levels of LDL-C levels beginning at birth, are at high-risk for cardiovascular events at an early age.[6] Heterozygous familial hypercholesterolemia is one of the most common genetic disorders, affecting approximately one out of every 300 to 500 people worldwide.[7]

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).

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. Phase 3 clinical trials for evolocumab are currently underway and build upon the Phase 2 studies.

The Phase 3 program includes 13 trials, with a combined planned enrollment of more than 28,000 patients. The Phase 3 studies will evaluate evolocumab administered every two weeks and monthly in multiple patient populations, including in combination with statins in patients with hyperlipidemia (LAPLACE-2), in patients with hyperlipidemia who cannot tolerate statins (GAUSS-2), as a stand-alone treatment in patients with hyperlipidemia (MENDEL-2), and in patients whose elevated cholesterol is caused by genetic disorders called heterozygous (RUTHERFORD-2) and homozygous (TESLA and TAUSSIG) familial hypercholesterolemia.

Five studies of evolocumab 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, and 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.

Additional information about clinical trials of evolocumab can be found at www.clinicaltrials.gov.

About Evolocumab

Evolocumab is a fully human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9).[2] 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.[8] 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.[2]

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 Jan. 30, 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.

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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(Logo: http://photos.prnewswire.com/prnh/20081015/AMGENLOGO)

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