



## Amgen Announces Positive Top-Line Results From Phase 3 LAPLACE-2 Trial Of Evolocumab (AMG 145) In Combination With Statins In Patients With High Cholesterol

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### Study Meets Co-Primary Endpoints of LDL Cholesterol Reduction

THOUSAND OAKS, Calif., Jan. 28, 2014 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the Phase 3 LAPLACE-2 (LDL-C Assessment with PCSK9 Monoclonal Antibody Inhibition Combined with Statin Therapy-2) trial evaluating evolocumab in combination with statin therapy in patients with high cholesterol 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 published results observed for the same doses in the Phase 2 LAPLACE-TIMI 57 (LAPLACE-Thrombolysis In Myocardial Infarction-57) trial for evolocumab compared to placebo; and in the Phase 2 MENDEL (Monoclonal Antibody Against PCSK9 to Reduce Elevated LDL-C in Patients Currently Not Receiving Drug Therapy For Easing Lipid Levels) study for evolocumab compared to ezetimibe.<sup>1-2</sup>

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.<sup>3</sup>

The LAPLACE-2 trial evaluated safety, tolerability and efficacy of evolocumab in combination with statin therapy compared to placebo and ezetimibe in 1,896 patients with high cholesterol. Patients were randomized to one of 24 treatment groups to compare subcutaneous evolocumab (140 mg every two weeks or 420 mg monthly) with subcutaneous placebo (every two weeks or monthly) or ezetimibe (10 mg daily) when added to different daily doses of statin therapies.

Safety was balanced across treatment groups. No adverse events (AEs) occurred in  $\geq 2$  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.

"As statins continue to be an important treatment option in patients with high cholesterol, we are very encouraged by the Phase 3 data from the LAPLACE-2 study," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Adding evolocumab to statin therapy may help patients control their LDL cholesterol levels when high doses of statins are not sufficient."

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

According to the Centers for Disease Control and Prevention, more than 71 million American adults have high LDL-C.<sup>4</sup> Elevated LDL-C is recognized as a major risk factor for cardiovascular disease.<sup>5-6</sup> A multinational survey of almost 10,000 patients with high cholesterol on statin therapy found approximately one-third of patients did not attain their LDL-C goal.<sup>7</sup>

### 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  $\geq 80$  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).

Reference above to the published Phase 2 MENDEL study results for evolocumab compared to ezetimibe is made because the Phase 2 MENDEL study included a randomized comparison to ezetimibe and the Phase 2 LAPLACE-TIMI 57 study did not.

### 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](http://www.clinicaltrials.gov).

### **About Evolocumab**

Evolocumab is a fully human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9).<sup>3</sup> 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.<sup>8</sup> 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.<sup>3</sup>

### **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](http://www.amgen.com) and follow us on [www.twitter.com/amgen](https://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. 28, 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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