Amgen Announces New Four-Year Outcomes Study To Examine Long-Term Effects Of Repatha® (evolocumab) In High-Risk Cardiovascular Disease (CVD) Patients Without Prior Heart Attack Or Stroke

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VESALIUS-CV is the Latest Study in Amgen's PROFICIO Clinical Program Investigating the Impact of Repatha on CVD in Multiple Patient Populations

Phase 3 Study Will Enroll High-Risk Patients who Have Significant Atherosclerotic Disease or Diabetes and are at High Risk for a First Cardiovascular Event

THOUSAND OAKS, Calif., March 15, 2019 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced plans to conduct VESALIUS-CV, a multinational clinical outcomes study for Repatha® (evolocumab) which will involve at least 13,000 patients worldwide at high risk of experiencing a first cardiovascular (CV) event, despite optimized treatment with lipid-lowering therapy.[1] The study will be the first to investigate long-term outcomes in this population with Repatha for a minimum of four years.[1]

Conducted in collaboration with the Brigham and Women's Hospital Thrombolysis in Myocardial Infarction (TIMI) Study Group, patient enrollment for VESALIUS-CV is due to begin in the second quarter of 2019. The multicenter, double-blind, randomized, placebo-controlled, parallel-group outcomes study will include high-risk patients who have not yet had a heart attack or stroke, but have coronary, cerebrovascular or peripheral arterial disease, who may have had interventions, such as a coronary arterial bypass graft (CABG) or stents, or who may have diabetes with indicators of increased CVD risk.[1]

"High cholesterol is the most important risk factor in coronary heart and vascular disease, but we know that recommended levels of LDL-C or 'bad' cholesterol are frequently not reached in very high-risk patients," said Robert Giugliano, M.D., principal investigator and a senior investigator at the TIMI Study Group at Brigham and Women's Hospital and Harvard Medical School. "The VESALIUS-CV study will explore the impact of evolocumab on major cardiovascular events, such as heart attack or stroke, in patients who are already receiving treatment for lipid lowering and cardiovascular disease, but remain at high-risk, allowing us to better understand the benefits of significant LDL-C lowering in multiple patient types."

Amgen and TIMI previously collaborated on the Repatha cardiovascular outcomes study (FOURIER), which demonstrated Repatha's efficacy in reducing low-density lipoprotein cholesterol (LDL-C) levels, as well as the relative risk for major CV events in high-risk patients with a history of heart attack or stroke.[2] VESALIUS-CV will build on these findings by exploring the potential benefit of Repatha in preventing a first heart attack or stroke in patients with some of the most significant risk factors for a first CV event.[1]

VESALIUS-CV is part of Amgen's PROFICIO (Program to Reduce LDL-C and cardiovascular Outcomes Following Inhibition of PCSK9 In different pOpulations) program. This program of clinical studies investigates the impact of Repatha on CVD across multiple populations. To date, the PROFICIO program consists of 36 trials including more than 38,000 patients worldwide.[3]

"PROFICIO represents our commitment to advancing the science of cardiovascular disease and improving the care of patients worldwide, and VESALIUS-CV is an important addition to this growing program," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "By continuing to invest in new scientific discovery through PROFICIO, we can help address some of the most significant unmet needs in patients at risk of life-changing cardiovascular events."

About VESALIUS-CV

VESALIUS-CV is a Phase 3, multicenter, double-blind, randomized, placebo-controlled, parallel-group outcomes study. At least 13,000 patients will be enrolled in the study globally, with at least 6,500 patients per treatment arm. Repatha (140 mg) or placebo will be self-administered subcutaneously every two weeks for a minimum of four years. Follow-up of all randomized patients is planned to continue for a minimum of four years and until a sufficient number of patients have experienced the composite endpoints. Two primary endpoints include time to coronary heart disease (CHD) death, myocardial infarction (MI), ischemic stroke (triple component); and time to CHD death, MI, ischemic stroke or any ischemia-driven arterial revascularization, whichever occurs first (quadruple component).

About Repatha® (evolocumab)

Repatha is a human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9). Repatha binds to PCSK9 and inhibits circulating PCSK9 from binding to the low-density lipoprotein (LDL) receptor (LDLR), preventing PCSK9-mediated LDLR degradation and permitting LDLR to recycle back to the liver cell surface. By inhibiting the binding of PCSK9 to LDLR, Repatha increases the number of LDLRs available to clear LDL from the blood, thereby lowering LDL-C levels.[4]

Repatha is approved in more than 60 countries, including the U.S., Japan, Canada and in all 28 countries that are members of the European Union. Applications in other countries are pending.

Important U.S. Product Information

Repatha is a PCSK9 (proprotein convertase subtilisin kexin type 9) inhibitor antibody indicated:

- to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease.
- as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia [HeFH]) to reduce low-density lipoprotein cholesterol (LDL-C).

- as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

The safety and effectiveness of Repatha have not been established in pediatric patients with HoFH who are younger than 13 years old or in pediatric patients with primary hyperlipidemia or HeFH.

Important U.S. Safety Information
Contraindication: Repatha is contraindicated in patients with a history of a serious hypersensitivity reaction to Repatha. Serious hypersensitivity reactions including angioedema have occurred in patients treated with Repatha.

Allergic reactions: Hypersensitivity reactions (e.g. angioedema, rash, urticaria) have been reported in patients treated with Repatha, including some that led to discontinuation of therapy. If signs or symptoms of serious allergic reactions occur, discontinue treatment with Repatha, treat according to the standard of care, and monitor until signs and symptoms resolve.

Adverse reactions: The most common adverse reactions (>5% of patients treated with Repatha and occurring more frequently than placebo) were: nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions.

From a pool of the 52-week trial and seven 12-week trials: Local injection site reactions occurred in 3.2% and 3.0% of Repatha-treated and placebo-treated patients, respectively. The most common injection site reactions were erythema, pain, and bruising.

Allergic reactions occurred in 5.1% and 4.7% of Repatha-treated and placebo-treated patients, respectively. The most common allergic reactions were rash (1.0% versus 0.5% for Repatha and placebo, respectively), eczema (0.4% versus 0.2%), erythema (0.4% versus 0.2%), and urticaria (0.4% versus 0.1%).

The most common adverse reactions in the Cardiovascular Outcomes Trial (>5% of patients treated with Repatha and occurring more frequently than placebo) were: diabetes mellitus (8.8% Repatha, 8.2% placebo), nasopharyngitis (7.8% Repatha, 7.4% placebo), and upper respiratory tract infection (5.1% Repatha, 4.8% placebo).

Among the 16,676 patients without diabetes mellitus at baseline, the incidence of new-onset diabetes mellitus during the trial was 8.1% in patients assigned to Repatha compared with 7.7% in those assigned to placebo.

Homozygous Familial Hypercholesterolemia (HoFH): The adverse reactions that occurred in at least two patients treated with Repatha and more frequently than placebo were: upper respiratory tract infection, influenza, gastroenteritis, and nasopharyngitis.

Immunogenicity: Repatha is a human monoclonal antibody. As with all therapeutic proteins, there is a potential for immunogenicity with Repatha.

Please contact Amgen Medinfo at 800-77-AMGEN (800-772-6436) or 844-REPATHA (844-737-2842) regarding Repatha® availability or find more information, including full Prescribing Information, at www.amgen.com and www.Repatha.com.

About Amgen in the Cardiovascular Therapeutic Area
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.[5] 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 robust 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 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 the current expectations and beliefs of Amgen. 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 reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

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. Even when clinical trials are successful, regulatory authorities may question the sufficiency for

approval of the trial endpoints we have selected. 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, including our devices, after they are on the market.

Our results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and 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. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. Further, 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, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our commercial products. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. 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 acquire other companies or products and to integrate the operations of companies we have acquired may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. Our stock price is volatile and may be affected by a number of events. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

The scientific information discussed in this news release relating to new indications for our products is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration for the products. The products are not approved for the investigational use(s) discussed in this news release, and no conclusions can or should be drawn regarding the safety or effectiveness of the products for these uses.

CONTACT: Amgen, Thousand Oaks
Jessica Akopyan, 805-447-0974 (Media)
Kristen Davis, 805-447-3008 (Media)
Arvind Sood, 805-447-1060 (Investors)

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