



## Amgen Announces New FOURIER Analysis Showing Benefit Of Repatha® (evolocumab) In High-Risk Patients Who Have Experienced A Recent Heart Attack

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### Additional FOURIER Analysis Shows Lowering LDL-C With Repatha Did Not Impair Patient-Reported Cognition

THOUSAND OAKS, Calif., Nov. 16, 2019 /PRNewswire/ -- Amgen today announced a new analysis from the Repatha® (evolocumab) cardiovascular outcomes (FOURIER) study that evaluates the effectiveness of Repatha in patients who have suffered a recent myocardial infarction (MI). The analysis showed that patients who experienced a recent MI (less than one year) were at higher risk of subsequent cardiovascular (CV) events compared to patients who had an MI over a year ago. In the analysis, the risk reduction for experiencing a heart attack, stroke or CV death, in Repatha-treated patients treated within one year post MI was 25% compared to 15% in those patients with a more distant MI. The results will be presented at the American Heart Association Annual Scientific Sessions in Philadelphia on Monday, Nov. 18.

"Nearly 1 in 5 patients will have a recurrent CV event during the first year after a heart attack which makes that year a critical time for high-risk patients<sup>1</sup>," said Robert Giugliano, M.D., FOURIER executive committee member and a senior investigator at the TIMI Study Group at Brigham and Women's Hospital and Professor of Medicine at Harvard Medical School. "These results demonstrate the importance of intensive lipid-lowering therapy in the first year following a heart attack and provide additional evidence that evolocumab significantly reduces CV risk and improves outcomes for high-risk patients."

In this analysis of the landmark FOURIER outcomes study, 5,711 patients who experienced an MI within one to 12 months of randomization were compared to 16,609 patients with a more distant event (>12 months prior to randomization) to assess the efficacy of Repatha on the primary endpoint (CV death, MI, stroke, unstable angina or coronary revascularization) and the key secondary endpoint (CV death, MI or stroke).

"Far too many patients remain at risk of another CV event because they are not managing one of the most important modifiable risk factors for a heart attack: high LDL-C<sup>2</sup>," said Darryl Sleep, M.D., senior vice president of Global Medical and chief medical officer at Amgen. "These data demonstrate the important role cardiologists play in closely monitoring and managing LDL-C in high-risk patients, and support recent professional guideline recommendations that call for more intensive reduction of LDL-C to lower the risk of future CV events in high-risk patients<sup>3,4</sup>."

### New FOURIER Data Shows No Impact on Patient-Reported Cognition Function

An additional analysis from the FOURIER study presented at AHA reinforces the safety and efficacy of intensive LDL-C lowering with Repatha in high-risk cardiovascular disease (CVD) patients. The analysis evaluated the impact of lowering LDL-C with Repatha on cognition as reported by patients with stable CVD and found that the addition of Repatha to statin therapy had no impact on reported everyday cognition function, including in those with very low LDL-C levels.

### PROFICIO Program

FOURIER is part of Amgen's PROFICIO (Program to Reduce LDL-C and cardiovascular Outcomes Following Inhibition of PCSK9 In different populations) program of clinical studies investigating the impact of Repatha on LDL-C and CVD across multiple populations at high CV risk, including those managed by statins, statin-intolerant patients, those with genetic disorders and patients with atherosclerosis. To date, the PROFICIO program consists of 36 trials including more than 38,000 patients worldwide.

### Repatha Cardiovascular Outcomes (FOURIER) Study Design

FOURIER (Further cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk), a multinational Phase 3 randomized, double-blind, placebo-controlled trial, was designed to evaluate whether treatment with Repatha in combination with statin therapy compared to placebo plus statin therapy reduces cardiovascular events. The primary endpoint was the time to cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization. The key secondary endpoint was the time to cardiovascular death, myocardial infarction or stroke.

Eligible patients with high cholesterol (LDL-C  $\geq$ 70 mg/dL or non-high-density lipoprotein cholesterol [non-HDL-C]  $\geq$ 100 mg/dL) and clinically evident atherosclerotic cardiovascular disease at more than 1,300 study locations around the world were randomized to receive Repatha subcutaneous 140 mg every two weeks or 420 mg monthly plus effective statin dose; or placebo subcutaneous every two weeks or monthly plus effective statin dose. Optimized statin therapy was defined as at least atorvastatin 20 mg or equivalent daily with a recommendation for at least atorvastatin 40 mg or equivalent daily where approved. The study was event-driven and continued until at least 1,630 patients experienced a key secondary endpoint.

### 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.<sup>5</sup>

Repatha is approved in more than 70 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](http://www.amgen.com) and [www.Repatha.com](http://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.<sup>6</sup> 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](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 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 any statements on the outcome, benefits and synergies of collaboration with any other company, including BeiGene, Ltd., or the acquisition of Otezla® (apremilast), including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion, as well as 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. 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. 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 collaborate with or acquire other companies or products, and to integrate the operations of companies or in support of products 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 any 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.

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