AMGEN PRESENTS NEW REPATHA® (EVOLOCUMAB) DATA AT AHA 2022

November 7, 2022

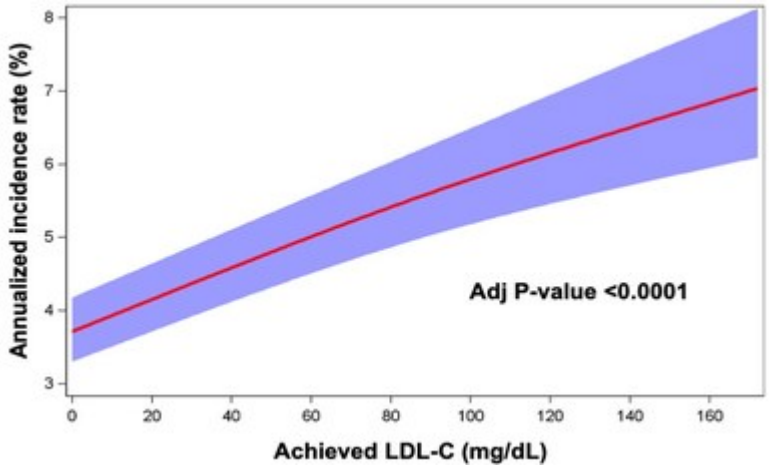
Very low LDL-C Levels <20 mg/dL Were Well Tolerated With no new Safety Signals and Were Associated With a Reduced Risk of Cardiovascular Outcomes

Data Reinforces Long-Term Efficacy and Consistent Safety Profile of Repatha Observed in FOURIER-OLE

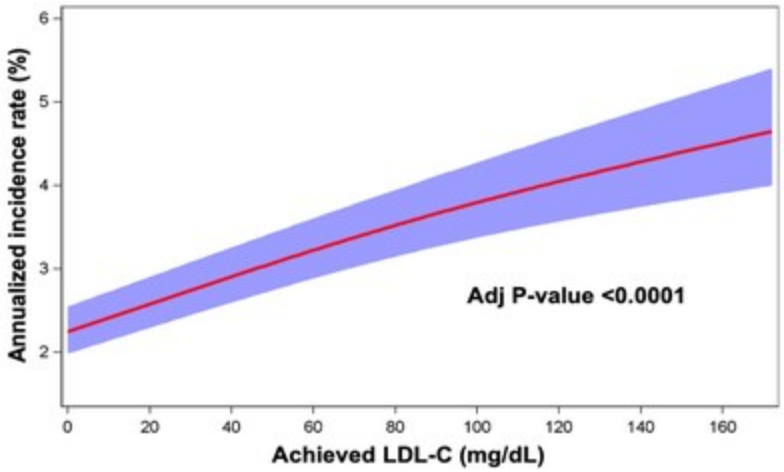
THOUSAND OAKS, Calif., Nov. 7, 2022 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today presented a new analysis from the Phase 3 FOURIER and FOURIER open label extension (OLE) studies of Repatha® (evolocumab) in adults with atherosclerotic cardiovascular disease (ASCVD) during the Nov. 7 Late-Breaking Science Session of the American Heart Association (AHA) Scientific Sessions 2022 in Chicago, Illinois. These data demonstrated that achieving and sustaining a low-density lipoprotein cholesterol (LDL-C) level of <20 mg/dL was associated with improved cardiovascular (CV) outcomes, including the composite endpoint of cardiovascular death, myocardial infarction (MI) and stroke, with no evidence of an increased incidence of safety events for up to 8.6 years of follow-up.[1]

"The current analysis further supports that achieving very low LDL-C long-term is not associated with any new safety signals and correlates with the reduction in cardiovascular events in patients with atherosclerotic cardiovascular disease," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "Repatha continues to be at the forefront of PCSK9i research, with the longest safety and efficacy trial data among PCSK9i treatments for cardiovascular disease, providing crucial information for patients and doctors managing this disease."

This pre-specified exploratory analysis examined the association between achievement of different LDL-C levels with the incidence of cardiovascular and safety outcomes for up to 8.6 years of follow up.[1] Between the parent FOURIER and FOURIER-OLE studies, over 3,500 patients (13%) achieved LDL-C levels of <20 mg/dL and over 10,000 (39%) achieved LDL-C levels of <40 mg/dL.[1] This analysis found that over the course of 77,470 patient-years of follow-up there was a monotonic relationship between lower LDL-C levels – down to very low LDL-C levels <20 mg/dL – and a lower risk of the efficacy endpoint from FOURIER of CV death, MI, stroke, coronary revascularization or hospital admission for unstable angina (see Figure 1).[1]



A similar relationship was observed between achieved LDL-C levels and the risk of the key secondary efficacy endpoint from FOURIER of CV death, MI or stroke (P for trend<0.0001) (see Figure 2).[1] There were no significant associations between lower achieved LDL-C and the risk of serious adverse events, neurocognitive events, the development of new onset diabetes, cataract-related adverse events, new or progressive malignancy, the occurrence of hemorrhagic stroke, muscle-related events or non-cardiovascular death.[1]



"Until now, there was a gap in the medical knowledge of the long-term efficacy and safety implications of a very low LDL-C level <20 mg/dL," said Marc S. Sabatine, MD, Chair of the TIMI Study Group at Brigham and Women's Hospital and senior investigator for this study. "These data fill that gap by demonstrating that a lower LDL-C level was associated with improved cardiovascular outcomes with a similar safety profile, down to very low LDL-C levels. Furthermore, these data substantiate the use of a PCSK9 inhibitor to reduce LDL-C below the threshold of 55 mg/dL for very high-risk ASCVD patients, as recommended in the recently published ACC 2022 Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-C Lowering in the Management of ASCVD Risk."

Prolonged LDL-C reduction with Repatha is also being studied in 12,301 patients without a prior heart attack or stroke in the ongoing VESALIUS-CV (NCT03872401) outcomes trial.

About Cardiovascular Disease (CVD)

CVD remains the leading cause of global mortality and a major contributor to disability and rising healthcare costs.[2,3] LDL-C is a key modifiable risk factor for the development of CVD, yet nearly half of post-MI patients fail to achieve guideline recommended LDL-C goals, including those taking high-intensity statins, leaving many patients at risk for another cardiovascular event.[4,5] Nearly one in five patients who have had a heart attack will have another cardiovascular event within one year, so it's important that patients get their LDL-C to guideline recommended levels.[6] The American College of Cardiology's recent Expert Consensus Decision Pathway reinforces the criticality of lowering LDL-C in an update to the previous guidelines, including a lower threshold of 55 mg/dL for very high-risk ASCVD patients, and underscores the important role that PCSK9 inhibitor mAbs, like Repatha, play in helping to prevent cardiovascular events, like heart attack and stroke.[7]

Repatha® FOURIER and FOURIER-OLE Study Design

FOURIER (20110118) was a multinational Phase 3 randomized, double-blind, placebo-controlled trial, designed to evaluate whether treatment with Repatha in combination with statin therapy compared to placebo plus statin therapy reduced cardiovascular events. The primary endpoint was the time to first occurrence of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization. The key secondary endpoint was the time to first occurrence of cardiovascular death, myocardial infarction or stroke.

Eligible patients with high cholesterol (LDL-C ≥70 mg/dL or non-high-density lipoprotein cholesterol [non-HDL-C] ≥100 mg/dL) and clinically evident ASCVD 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.

FOURIER-OLE were multicenter, open-label extension studies designed to assess the extended long-term safety of evolocumab in subjects who completed the FOURIER study. The FOURIER-OLE was composed of studies 20130295 and 20160250, which enrolled 5,035 and 1,600 subjects who completed the FOURIER study to receive open-label evolocumab and were followed up for a median of 5 and 4.6 years, respectively. All patients in the extension program were treated with open label evolocumab resulting in no concurrent placebo arm during this period. Although not all patients participated in FOURIER-OLE, baseline characteristics were broadly comparable between the originally randomized treatment arms, thereby allowing for reasonably unconfounded exploratory comparisons between groups.

Total of 26,389 patients had an early achieved LDL-C available, 19,960 of whom were in FOURIER alone with a median follow-up of 2.0 years and 6,429 of whom also participated in FOURIER-OLE with a median follow-up of ~7 years and a maximum follow-up of 8.6 years.

PROFICIO Program

FOURIER and its extension studies are 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 50 trials including more than 51,000 patients worldwide.

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 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 one of the world's leading independent biotechnology companies,

has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

Amgen is one of the 30 companies that comprise the Dow Jones Industrial Average and is also part of the Nasdaq-100 index. In 2022, Amgen was named one of the "World's Best Employers" by Forbes and one of "America's 100 Most Sustainable Companies" by Barron's.

For more information, visit Amgen.com and follow us on Twitter, LinkedIn, Instagram, TikTok and YouTube.

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. The clinical benefits and safety of Repatha have been studied for 12 years in 50 clinical trials with over 47,000 patients. This vast body of evidence demonstrates that Repatha works rapidly.

Repatha is approved in more than 75 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[8]

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

- in adults with established cardiovascular disease to reduce the risk of myocardial infarction, stroke, and coronary revascularization
- as an adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDLC)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C
- as an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 10 years and older with HeFH, to reduce LDL-C
- as an adjunct to other LDL-C-lowering therapies in adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH), to reduce LDL-C

The safety and effectiveness of Repatha have not been established in pediatric patients with HeFH or HoFH who are younger than 10 years old or in pediatric patients with other types of hyperlipidemia or HeFH.

Important U.S. Safety Information[8]

INDICATIONS
Repatha® is indicated:

- In adults with established cardiovascular disease to reduce the risk of myocardial infarction, stroke, and coronary revascularization
- As an adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)–lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL–C
- As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 10 years and older with HeFH, to reduce LDL-C
- As an adjunct to other LDL–C-lowering therapies in adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH), to reduce LDL–C

The safety and effectiveness of Repatha® have not been established in pediatric patients with HeFH or HoFH who are younger than 10 years old or in pediatric patients with other types of hyperlipidemia.

IMPORTANT SAFETY INFORMATION

- **Contraindication:** Repatha® is contraindicated in patients with a history of a serious hypersensitivity reaction to evolocumab or any of the excipients in Repatha®. Serious hypersensitivity reactions including angioedema have occurred in patients treated with Repatha®.

- **Hypersensitivity Reactions:** Hypersensitivity reactions, including angioedema, have been reported in patients treated with Repatha®. If signs or symptoms of serious hypersensitivity reactions occur, discontinue treatment with Repatha®, treat according to the standard of care, and monitor until signs and symptoms resolve.

- **Adverse Reactions in Adults with Primary Hyperlipidemia:** The most common adverse reactions (>5% of patients treated with Repatha® and 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. Hypersensitivity reactions occurred in 5.1% and 4.7% of Repatha®-treated and placebo-treated

patients, respectively. The most common hypersensitivity 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%).

- **Adverse Reactions in the Cardiovascular Outcomes Trial:** The most common adverse reactions (>5% of patients treated with Repatha® and 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 treated with Repatha® compared with 7.7% in patients that received placebo.

- **Adverse Reactions in Pediatric Patients with HeFH:** The most common adverse reactions (>5% of patients treated with Repatha® and more frequently than placebo) were: nasopharyngitis, headache, oropharyngeal pain, influenza, and upper respiratory tract infection.

- **Adverse Reactions in Adults and Pediatric Patients with HoFH:** In a 12-week study in 49 patients, 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. In an open-label extension study in 106 patients, including 14 pediatric patients, no new adverse reactions were observed.

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

Please see full Prescribing Information.

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.

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 collaborations, or potential collaborations, with any other company (including BeiGene, Ltd., Kyowa-Kirin Co., Ltd., or any collaboration to manufacture therapeutic antibodies against COVID-19), the performance of Otezla® (apremilast) (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), the Five Prime Therapeutics, Inc. acquisition, or the Teneobio, Inc. acquisition, or the ChemoCentryx, Inc. acquisition, 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, effects of pandemics or other widespread health problems such as the ongoing COVID-19 pandemic on our business, 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. An outbreak of disease or similar public health threat, such as COVID-19, and the public and governmental effort to mitigate against the spread of such disease, could have a significant adverse effect on the supply of materials for our manufacturing activities, the

distribution of our products, the commercialization of our product candidates, and our clinical trial operations, and any such events may have a material adverse effect on our product development, product sales, business and results of operations. 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, products or technology, and to integrate the operations of companies or to support the products or technology 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 and operations may be negatively affected by the failure, or perceived failure, of achieving our environmental, social and governance objectives. The effects of global climate change and related natural disasters could negatively affect our business and operations. Global economic conditions may magnify certain risks that affect our business. 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 related to our product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates. Further, any 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.

References

1. Sabatine, Marc (2022, November 5-7). *Long-Term Efficacy of Very Low LDL-Cholesterol Levels With the PCSK9 Inhibitor Evolocumab: Analysis of the FOURIER and FOURIER-OLE Studies* [Conference Presentation]. American Heart Association Scientific Sessions, Chicago, Illinois.
2. World Health Organization. Cardiovascular diseases (CVDs) fact sheet. http://www.who.int/mediacentre/factsheets/fs317/en/. Accessed August 2022.
3. The American College of Cardiology. (2020, December 9). *Cardiovascular Disease Burden, Deaths Are Rising Around the World*. [Press Release]. Retrieved from https://www.acc.org/about-acc/press-releases/2020/12/09/18/30/cvd-burden-and-deaths-rising-around-the-world.
4. Understand your risks to prevent a heart attack. www.heart.org. (2022, February 10). Retrieved October 25, 2022, from https://www.heart.org/en/health-topics/heart-attack/understand-your-risks-to-prevent-a-heart-attack.
5. Baum, S. J., Rane, P. B., Nunna, S., Habib, M., Philip, K., Sun, K., Wang, X., & Wade, R. L. (2021). Geographic variations in lipid-lowering therapy utilization, LDL-C levels, and proportion retrospectively meeting the ACC/AHA very high-risk criteria in a real-world population of patients with major atherosclerotic cardiovascular disease events in the United States. *American journal of preventive cardiology*, *6*, 100177. https://doi.org/10.1016/j.ajpc.2021.100177.
6. Jernberg T, Hasvold P, Henriksson M, et al. Cardiovascular risk in post-myocardial infarction patients: nationwide real world data demonstrate the importance of a long-term perspective. https://academic.oup.com/eurheartj/article/36/19/1163/2293202. Accessed 25 October 2022.
7. Lloyd-Jones, D. M., Morris, P. B., & Ballantyne, C. M., et al. (2022). 2022 ACC expert consensus decision pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk. *Journal of the American College of Cardiology*. https://doi.org/10.1016/j.jacc.2022.07.006.
8. Repatha® U.S. Prescribing Information; Amgen, Thousand Oaks, CA, 2021.

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