NEW AMGEN DATA AT ESC 2022 SHOW LONG-TERM LDL-C LOWERING WITH REPATHA® (EVOLOCUMAB) WAS WELL-TOLERATED FOR MORE THAN 8 YEARS

August 29, 2022

Earlier Treatment With Repatha Resulted in a Lower Incidence of Major CV Events, Including CV Death

80% of Patients Achieved Guideline Directed LDL-C Levels of <55 mg/dL at Week 12

Data Presented at ESC 2022 and Simultaneously Published in *Circulation*

THOUSAND OAKS, Calif., Aug. 29, 2022 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today presented new compelling data from the Phase 3 FOURIER open label extension (OLE) studies of Repatha® (evolocumab) in adults with atherosclerotic cardiovascular disease (ASCVD) during the Aug. 29 late-breaking Hot Line Session of the European Society of Cardiology (ESC) Annual Meeting being held in Barcelona, Spain, and online. These data were simultaneously published in *Circulation*. Repatha is the first and only proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9i) to date to show long-term clinical outcomes in patients with ASCVD for up to 8.4 years.[1]

To view the Multimedia News Release, please visit: https://www.multivu.com/players/English/8812855-new-amgen-data-esc-2022/

The FOURIER-OLE studies evaluated 6,635 patients from the FOURIER parent study (3,355 initially randomized to Repatha and 3,280 to placebo) from the U.S. and Europe.[1] The studies were designed to assess the long-term safety and tolerability of Repatha in adults with clinically evident ASCVD for a median follow up of up to five years and a maximum exposure to Repatha of more than eight years when parent and extension studies were combined. No new long-term safety findings were observed.[1]

The OLE studies showed Repatha delivered medically significant and sustained reduction in low-density lipoprotein cholesterol (LDL-C) levels, with 80% of patients achieving a low-density lipoprotein cholesterol (LDL-C) level of <55mg/dL.[1] Additionally, the LDL-C reduction of 58% from baseline was consistent over long-term follow up (week 260) on Repatha. An additional prespecified exploratory analysis in the OLE studies showed a lower rate of major adverse cardiovascular events, including cardiovascular death, in patients originally randomized to Repatha (20% relative risk reduction [RRR] for major cardiovascular events and 23% RRR for cardiovascular death) versus those originally randomized to placebo in the parent FOURIER study.[1]

"The new findings from the FOURIER-OLE studies confirm that earlier initiation of Repatha, combined with longer duration of treatment, has the potential to deliver a greater reduction in cardiovascular risk, including death," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "These data add to the robust body of evidence for Repatha, demonstrating that long-term treatment with Repatha is well tolerated in patients with stable ASCVD."

"These findings fill a significant gap in the body of research on the long-term safety and efficacy of PCSK9 inhibitors," said Michelle L. O'Donoghue M.D., MPH, senior investigator, TIMI Study Group at Brigham and Women's Hospital and Lead FOURIER-OLE Trial Investigator. "Importantly, earlier initiation of LDL-C lowering with evolocumab combined with consistent long-term use, further reduced the risk of major cardiovascular events and cardiovascular mortality in this study."

Cardiovascular disease (CVD) remains the leading cause of global mortality and a major contributor to disability and rising healthcare costs.[2,3] In the U.S., someone suffers a heart attack every 40 seconds.[4] Given systemic barriers in the U.S. healthcare system, only 3.2% of an estimated 18.7 million U.S. adults with ASCVD were actually taking an add-on lipid-lowering therapy, despite treatment being recommended to 61.4%.[5] Further, patients with ASCVD whose prescription for a PCSK9i was rejected had an 11% higher risk of having a cardiovascular event such as a heart attack or stroke within a year.[6]

"LDL-C is a key modifiable risk factor for the development of cardiovascular disease, yet nearly half of post-MI patients fail to achieve guideline recommended LDL-C goals of <70 mg/dL, including those taking high-intensity statins, leaving many patients at risk for another cardiovascular event," said Katherine Wilemon, founder and chief executive officer, Family Heart Foundation. "Nearly 1 in 5 patients who have had a heart attack will have another cardiovascular event within 1 year, so it's important that patients get their LDL-C to guideline recommended levels. With this new data, it's clear that Repatha can help patients achieve lower levels of LDL-C."

Detailed study results will be shared with regulatory authorities. Prolonged LDL-C reduction with Repatha is also being studied in patients without a prior heart attack or stroke in the ongoing VESALIUS-CV (NCT03872401) outcomes trial.

Repatha® Cardiovascular Open-Label Extension (FOURIER-OLE) Study Design

FOURIER (20110118) was a randomized placebo-controlled study of evolocumab, in patients with clinically evident ASCVD on stable effective statin therapy. 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 (20110118). The FOURIER-OLE is composed of studies 20130295 and 20160250, which enrolled 5,035 and 1,600 subjects who completed the FOURIER study (20110118) 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.

FOURIER Study Design

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

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.

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 2021, Amgen was named one of the 25 World's Best Workplaces™ by Fortune and Great Place to Work™ and one of the 100 most sustainable companies in the world by Barron's.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

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 EU Product Information[7]

In Europe, Repatha is approved for use in:

Hypercholesterolaemia and mixed dyslipidaemia Repatha is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non–familial) or mixed dyslipidaemia, as an adjunct to diet:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL–C goals with the maximum tolerated dose of a statin or,
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

Homozygous familial hypercholesterolaemia Repatha is indicated in adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies.

Established atherosclerotic cardiovascular disease Repatha is indicated in adults with established atherosclerotic cardiovascular disease (myocardial infarction, stroke or peripheral arterial disease) to reduce cardiovascular risk by lowering LDL-C levels, as an adjunct to correction of other risk factors:

- in combination with the maximum tolerated dose of a statin with or without other lipid-lowering therapies or,
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

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Primary hypercholesterolaemia and mixed dyslipidaemia in adults
The recommended dose of Repatha is either 140 mg every two weeks or 420 mg once monthly; both doses are clinically equivalent.

Homozygous familial hypercholesterolaemia in adults and adolescents aged 12 years and over
The initial recommended dose is 420 mg once monthly. After 12 weeks of treatment, dose frequency can be up–titrated to 420 mg once every 2 weeks if a clinically meaningful response is not achieved. Patients on apheresis may initiate treatment with 420 mg every two weeks to correspond with their apheresis schedule.

Established atherosclerotic cardiovascular disease in adults
The recommended dose of Repatha is either 140 mg every two weeks or 420 mg once monthly; both doses are clinically equivalent.

Important Safety Information
This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Special Warnings and Precautions: Renal impairment: There is limited experience with Repatha in patients with severe renal impairment (defined as eGFR < 30 mL/min/1.73 m^2). Repatha should be used with caution in patients with severe renal impairment. Hepatic impairment: In patients with moderate hepatic impairment, a reduction in total evolocumab exposure was observed that may lead to a reduced effect on LDL-C reduction. Therefore, close monitoring may be warranted in these patients. Patients with severe hepatic impairment (Child-Pugh C) have not been studied. Repatha should be used with caution in patients with severe hepatic impairment. Dry natural rubber: The needle cover of the glass pre-filled syringe and of the pre-filled pen is made from dry natural rubber (a derivative of latex), which may cause allergic reactions. Sodium content: Repatha contains less than 1 mmol sodium (23 mg) per dose, i.e. it is essentially 'sodium-free'.

Interactions: No formal drug-drug interaction studies have been conducted for Repatha. No studies on pharmacokinetic and pharmacodynamics interaction between Repatha and lipid-lowering drugs other than statins and ezetimibe have been conducted.

Fertility, Pregnancy and Lactation: There are no or limited amount of data from the use of Repatha in pregnant women. Repatha should not be used during pregnancy unless the clinical condition of the woman requires treatment with evolocumab. It is unknown whether evolocumab is excreted in human milk. A risk to breastfed newborns/infants cannot be excluded. No data on the effect of evolocumab on human fertility are available.

Undesirable Effects: The following common (≥ 1/100 to < 1/10) adverse reactions have been reported in pivotal, controlled clinical studies: influenza, nasopharyngitis, upper respiratory tract infection, rash, nausea, back pain, arthralgia, injection site reactions. Please consult the SmPC for a full description of undesirable effects.

Pharmaceutical Precautions: Store in a refrigerator (2 degrees C – 8 degrees C). Do not freeze. Keep the pre-filled syringe or the pre-filled pen in the original carton in order to protect from light. If removed from the refrigerator, Repatha may be stored at room temperature (up to 25 degrees C) in the original carton and must be used within 1 month.

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]

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).

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.

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 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 recently announced proposed acquisition of ChemoCentryx, Inc., 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.

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CONTACT: Amgen, Thousand Oaks
Michael Strapazon, 805-313-5553 (media)
Jessica Akopyan, 805-440-5721 (media)
Arvind Sood, 805-573-4142 (investors)