



Amgen To Present Robust Data Exploring The Impact Of Treatment With Repatha® (evolocumab) Across Patient Subgroups And High-Risk Populations At ESC Congress 2018

August 21, 2018

New Research Evaluates the Benefit of LDL-C Lowering With Repatha Across Gender and Age Data Assesses the Financial Burden for Patients in Europe With Atherosclerotic Cardiovascular Disease

THOUSAND OAKS, Calif., Aug. 21, 2018 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced the upcoming presentation of new Repatha® (evolocumab) analyses, including a late-breaking study evaluating the efficacy of Repatha in patients with metabolic syndrome and established cardiovascular disease at the ESC Congress 2018, organized by the European Society of Cardiology, in Munich, Aug. 25-29.

Six abstracts, including two analyses from the Repatha cardiovascular outcomes study (FOURIER), will be presented, providing further insight into the efficacy and safety of Repatha among a variety of patient groups. Data on the residual risk and financial burden for patients with atherosclerotic cardiovascular disease (ASCVD) across Europe will also be presented.

"For some high-risk patients, statins and other traditional lipid-lowering therapies are not enough to reduce elevated low-density lipoprotein cholesterol (LDL-C). This is particularly critical in patients who have had multiple events or a recent cardiovascular event. Data to be presented at ESC Congress 2018 reinforces the role of Repatha as a proven, effective and safe treatment option for these patients," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "Amgen continues to build a robust body of clinical evidence that demonstrates Repatha provides extremely potent LDL lowering efficacy and is, therefore, of high clinical and economic value."

A full list of Amgen-sponsored abstracts at ESC Congress 2018 can be found [online](#) and below:

Evolocumab Research Late-Breaking Science Session

- **FOURIER - Efficacy of PCSK9 inhibition with evolocumab in patients with Metabolic Syndrome**
Late Breaking Pharmacological Science, Saturday, Aug. 25, 11 a.m. - 12:30 p.m. CEST

Oral Presentation

- **Benefit of LDL-C lowering with evolocumab on cardiovascular outcomes by age & sex: an analysis of the FOURIER trial**
PCSK9 inhibitors - for the many or the few? Tuesday, Aug. 28, 8:30 a.m. - 10 a.m. CEST

Poster Sessions

- **Residual risk following myocardial infarction despite intensive medical management**
Poster Session 1: Antiplatelet and anticoagulant drugs, Saturday, Aug. 25, 11 a.m. - 4 p.m. CEST
- **Assessment of cardiovascular disease risk using different thresholds to define high risk on the pooled cohort equations**
Atrial fibrillation, stroke and cardiovascular risk, Saturday, Aug. 25, 12:35 p.m. - 1:25 p.m. CEST
- **Characteristics of patients prescribed evolocumab in Europe, Does clinical use match clinical guidelines?**
Poster Session 2: Coronary artery disease epidemiology and outcomes, Sunday, Aug. 26, 8:30 a.m. - 12:30 p.m. CEST
- **Patient and caregiver productivity loss and indirect costs associated with cardiovascular events in Europe**
Poster Session 3: Health economics, Sunday, Aug. 26, 2 p.m. - 6 p.m. CEST

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, 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 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.¹

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 EU Product Information

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 m²). 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 ($\geq 1/100$ 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

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.

Allergic reactions: Hypersensitivity reactions (e.g. 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 percent of Repatha-treated patients and occurring more frequently than placebo) in controlled trials involving patients with primary hyperlipidemia, including HeFH, were: nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions.

In a 52-week trial, adverse reactions led to discontinuation of treatment in 2.2 percent of Repatha-treated patients and 1 percent of placebo-treated patients. The most common adverse reaction that led to Repatha treatment discontinuation and occurred at a rate greater than placebo was myalgia (0.3 percent versus 0 percent for Repatha and placebo, respectively).

Adverse reactions from a pool of the 52-week trial and seven 12-week trials: Local injection site reactions occurred in 3.2 percent and 3.0 percent of Repatha-treated and placebo-treated patients, respectively. The most common injection site reactions were erythema, pain, and bruising. The proportions of patients who discontinued treatment due to local injection site reactions in Repatha-treated patients and placebo-treated patients were 0.1 percent and 0 percent, respectively.

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

The safety profile of Repatha in the cardiovascular outcomes trial was generally consistent with the safety profile in the 12- and 52-week controlled trials involving patients with primary hyperlipidemia, including HeFH. Serious adverse events occurred in 24.8 percent and 24.7 percent of Repatha-treated and placebo-treated patients, respectively. Adverse events led to discontinuation of study treatment in 4.4 percent of patients assigned to Repatha and 4.2 percent assigned to placebo. Common adverse reactions (>5 percent of patients treated with Repatha and occurring more frequently than placebo) included diabetes mellitus (8.8 percent Repatha, 8.2 percent placebo), nasopharyngitis (7.8 percent Repatha, 7.4 percent placebo) and upper respiratory tract infection (5.1 percent Repatha, 4.8 percent placebo). Among the 16,676 patients without diabetes mellitus at baseline, the incidence of new-onset diabetes mellitus during the trial was 8.1 percent in patients assigned to Repatha compared with 7.7 percent in those assigned to placebo.

Homozygous Familial Hypercholesterolemia (HoFH): In 49 patients with homozygous familial hypercholesterolemia studied in a 12-week, double-blind, randomized, placebo-controlled trial, 33 patients received 420 mg of Repatha subcutaneously once monthly. The adverse reactions that occurred in at least 2 (6.1 percent) Repatha-treated patients and more frequently than in placebo-treated patients, included upper respiratory tract infection (9.1 percent versus 6.3 percent), influenza (9.1 percent versus 0 percent), gastroenteritis (6.1 percent versus 0 percent), and nasopharyngitis (6.1 percent versus 0 percent).

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.² 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 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. 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. 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 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 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. 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. Discovery or identification of new product candidates cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate will be successful and become a commercial product. 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.

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References

1. Repatha Prescribing Information; Amgen, Thousand Oaks, CA, 2017.
2. World Health Organization. Cardiovascular diseases (CVDs) fact sheet. <http://www.who.int/mediacentre/factsheets/fs317/en/>. Accessed June 20, 2018.



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