

## News Release

**Amgen Canada Inc.**  
6775 Financial Dr.  
Mississauga, ON L5N 0A4  
Telephone 905-285-3000  
[www.Amgen.ca](http://www.Amgen.ca)

---

Please note: This information is for Canadian media only

### **NEW STUDY RESULTS OF REPATHA™ (EVOLOCUMAB) IN STATIN-INTOLERANT PATIENTS PUBLISHED IN *JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION***

**Data Simultaneously Presented in Late-Breaking Session at ACC.16**

**Repatha Shown to Significantly Reduce LDL-C by approximately 55  
per cent after 24 weeks compared to ezetimibe**

MISSISSAUGA, ON (April 4, 2016) – Amgen Canada Inc. today announced new detailed data from the Phase 3 GAUSS-3 (Goal Achievement After Utilizing an Anti-PCSK9 Antibody in Statin Intolerant Subjects-3) trial evaluating Repatha™ (evolocumab) in patients with high cholesterol who cannot tolerate statins. The study showed that in patients with reproducible statin intolerance due to muscle-related side effects (MRSE), the use of Repatha compared to ezetimibe resulted in a significant reduction in low-density lipoprotein cholesterol (LDL-C) after 24 weeks.<sup>1</sup> These data were presented yesterday at a Late-Breaking Clinical Trial session at the American College of Cardiology's 65<sup>th</sup> Annual Scientific Session (ACC.16) and simultaneously published in the *Journal of the American Medical Association*.

Data from prespecified co-primary endpoints showed the mean LDL-C reduction from baseline at weeks 22 and 24 was 54.5 per cent for Repatha compared to 16.7 per cent for ezetimibe ( $p < 0.001$ ). At week 24, LDL-C reduction was 52.8 per cent for Repatha compared to 16.7 per cent for ezetimibe ( $p < 0.001$ ). At baseline, the mean LDL-C level was 5.69 mmol/L for all patients entering the active-controlled part of the trial. Muscle-related side effects were reported in 20.7 per cent of Repatha patients vs 28.8 per cent of ezetimibe-patients. In patients treated with ezetimibe, active study drug was stopped for muscle symptoms in 6.8 per cent of patients, compared to 0.7 per cent of patients treated with Repatha.<sup>1</sup>

“Statin-related side effects can prevent some patients from achieving the desired reduction in LDL cholesterol levels, leaving them at risk for cardiovascular disease,” said Clive Ward-Able, executive director of Research and Development at Amgen Canada.



“This study has shown the efficacy and safety of Repatha consistent with the other GAUSS studies.”

The GAUSS-3 study built upon knowledge gained from the GAUSS-1 and GAUSS-2 studies, which used patient-reported incidence of statin-related side effects. GAUSS-3 employed a rigorous active statin rechallenge in patients with history of intolerance to two or more statins to determine a patient population that experienced MRSE on statin therapy but not on placebo. Despite the short, 10-week rechallenge, more than 40 per cent of patients rechallenged with atorvastatin developed intolerable muscle side effects to atorvastatin and not placebo.<sup>1</sup>

“This study helped to scientifically examine and evaluate muscle-related side-effects experienced by some patients receiving statin therapy,” said Dr. Jean Bergeron, MD, FRCPC, Director, Lipid Clinic, Centre Hospitalier Universitaire de Québec – Université Laval, Québec City. “Further, the study results demonstrate that a subset of patients who experience muscle-related side effects may benefit from an alternative therapy, Repatha, to lower LDL-C.”

In the GAUSS-3 trial there were no new safety findings. The most common adverse events that occurred in greater than 5 per cent of patients in the Repatha group were myalgia (13.8 per cent Repatha; 21.9 per cent ezetimibe), nasopharyngitis (9.7 per cent Repatha; 2.7 per cent ezetimibe), muscle spasms (9.0 per cent Repatha; 6.8 per cent ezetimibe), arthralgia (9.0 per cent Repatha; 1.4 per cent ezetimibe), pain in extremity (9.0 per cent Repatha; 1.4 per cent ezetimibe), fatigue (8.3 per cent Repatha; 6.8 per cent ezetimibe), headache (6.9 per cent Repatha; 9.6 per cent ezetimibe) and back pain (6.9 per cent Repatha; 8.2 per cent ezetimibe).<sup>1</sup>

### **GAUSS-3 Study Design<sup>1</sup>**

GAUSS-3 (Goal Achievement After Utilizing an Anti-PCSK9 Antibody in Statins Intolerant Subjects-3) is a Phase 3, multicenter, randomized, double-blind, placebo-controlled statin rechallenge trial designed to evaluate the safety, tolerability and efficacy of Repatha in 491 patients with high cholesterol who could not tolerate statins due to MRSE.

The study was divided into three parts (A, B, C):

- Part A was a two-period, double-blind, placebo-controlled, 24-week cross-over rechallenge of atorvastatin 20 mg in 491 patients with a history of statin intolerance to confirm the presence of statin-related MRSE. In Part A, patients were randomized in a 1:1 ratio to receive either atorvastatin 20 mg daily or oral placebo daily for 10 weeks (period one) before undergoing a two-week washout procedure and crossing over to the alternate therapy for a second 10 weeks (period two).
  - Upon completion of both periods one and two in Part A, patients who reported MRSE on atorvastatin and absence of MRSE on placebo entered into another two-week washout period and advanced to Part B. Patients



who did not develop MRSE on atorvastatin or developed MRSE on placebo were removed from the study.

- During Part A, patients who experienced a creatine kinase (CK) elevation >10x upper limit of normal (ULN) accompanied by muscle symptoms, with resolution of both CK elevation and muscle symptoms upon discontinuation of statin therapy, were considered the equivalent of intolerable MRSE and also advanced to Part B.
- Part B was a 24-week double-blind, double-dummy, active-controlled comparison of Repatha and ezetimibe in 218 patients. In Part B, patients were re-randomized 2:1 to receive either subcutaneous Repatha 420 mg once monthly and daily oral placebo or oral ezetimibe 10 mg daily and subcutaneous placebo monthly through week 48.
- Part C is an ongoing, two-year, open-label extension, during which all patients who completed Part B receive Repatha to evaluate its long-term safety and efficacy in patients with objectively-documented statin intolerance. All patients in the open-label extension portion receive subcutaneous Repatha 140 mg every two weeks or 420 mg once monthly. Data from the open label extension may be subject of a future presentation or publication.

The co-primary endpoints were the mean per cent reductions from baseline in LDL-C at weeks 22 and 24 and the per cent reduction from baseline in LDL-C at week 24 in Part B. Secondary efficacy endpoints included means at weeks 22 and 24 and at week 24 for the following: change from baseline in LDL-C; LDL-C response 1.8 mmol/L; change from baseline in total cholesterol (TC); change from baseline in non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (ApoB), TC/HDL-C ratio, ApoB/apolipoprotein A1 (ApoA1) ratio, lipoprotein(a), triglycerides, HDL-C and very low-density lipoprotein cholesterol (VLDL-C).<sup>1</sup>

### **About Repatha<sup>®</sup>™ (evolocumab)**

Repatha (evolocumab) is a fully human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9).<sup>2</sup> Repatha binds with high affinity 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>3</sup>

Repatha is indicated as an adjunct to diet and maximally tolerated statin therapy in adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of LDL-C; and as an adjunct to diet and other LDL-lowering therapies in adults and adolescent patients aged 12 and over with homozygous familial hypercholesterolemia (HoFH), who require additional lowering of LDL-C. The effect of Repatha on cardiovascular morbidity and mortality has not been determined.<sup>3</sup>



### **About Amgen Cardiovascular**

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>4</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 Canada**

As a leader in innovation, Amgen Canada understands the value of science. With main operations located in Mississauga, Ont.'s vibrant biomedical cluster, and its research facility in Burnaby, B.C., Amgen Canada has been an important contributor to advancements in science and innovation in Canada since 1991. The company contributes to the development of new therapies and new uses for existing medicines in partnership with many of Canada's leading health-care, academic, research, government and patient organizations. To learn more about Amgen Canada, visit [www.amgen.ca](http://www.amgen.ca).

### **Forward-Looking Statements**

This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen Inc. and its subsidiaries (Amgen, we or us) and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. 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 (SEC) reports filed by Amgen Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'s most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Amgen is providing this information as of April 4, 2016 and expressly disclaims any duty to update information contained in this news release.

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 and our partners to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. 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 after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. 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. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products (including products of our wholly-owned subsidiaries) are affected by the 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 as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of our products. In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, while we and our partners routinely obtain patents for our and their products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by our or our partners' competitors and there can be no guarantee of our or our partners' ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, 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 integrate the operations of companies we have acquired may not be successful. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our ongoing restructuring plan. 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 common stock.

###

**CONTACT:**

Natasha Bond, Head of Corporate Affairs  
Amgen Canada  
905-285-3007  
natasha.bond@amgen.com

Anjum Nayyar, Senior Consultant  
Hill+Knowlton Strategies  
416-413-4759  
Anjum.nayyar@hkstrategies.ca

**References**

1. Nissen SE, Stroes E, Dent-Acosta RE, et al. Efficacy and Tolerability of Evolocumab vs Ezetimibe in Patients With Muscle-Related Statin Intolerance: The GAUSS-3 Randomized Clinical Trial. *JAMA*. 2016;E1-E11.
2. Amgen Data on File, Investigator Brochure.
3. Repatha™ Product Monograph. Amgen Canada Inc. (September 2015).
4. World Health Organization. Cardiovascular diseases (CVDs) fact sheet. <http://www.who.int/mediacentre/factsheets/fs317/en/>. Accessed May 2015.