



## FDA Approves First And Only Single Monthly Injection For A PCSK9 Inhibitor

July 11, 2016

### Repatha® (evolocumab) Pushtronex™ System Available to U.S. Patients in Early August

THOUSAND OAKS, Calif., July 11, 2016 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the U.S. Food and Drug Administration (FDA) has approved the Repatha® (evolocumab) *Pushtronex*™ system (on-body infusor with prefilled cartridge), a new, monthly single-dose administration option.<sup>1</sup> The *Pushtronex* system is a hands-free device designed to provide 420 mg of Repatha in a single dose. Repatha is a human monoclonal antibody that blocks a protein called proprotein convertase subtilisin/kexin type 9 (PCSK9), which inhibits the body's natural system for eliminating "bad" cholesterol (low-density lipoprotein cholesterol or LDL-C) from the blood.<sup>1</sup> Repatha is the first and only PCSK9 inhibitor to offer a monthly single-dose delivery option.



### Repatha® (evolocumab) *Pushtronex*™ system (on-body infusor with prefilled cartridge)

"The *Pushtronex* system exemplifies Amgen's continued innovation and commitment to patients," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Repatha is the only PCSK9 inhibitor with an approved monthly dose, and now the only one with a monthly single-dose administration. The FDA approval of the *Pushtronex* system offers another delivery option to patients who need the additional LDL cholesterol lowering that Repatha can provide."

In the U.S., Repatha is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of LDL-C; and as an adjunct to diet and other LDL-lowering therapies for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) over age 13, who require additional lowering of LDL-C.<sup>1</sup> The effect of Repatha on cardiovascular morbidity and mortality has not been determined.

The new, single-use device was developed in collaboration with West Pharmaceutical Services, based on the SmartDose® technology platform, to provide patients with an additional dosing option for Repatha treatment. The device adheres to the body and patients are hands free during administration. Patients are able to perform moderate physical activities (such as walking, reaching or bending) as the 420 mg of Repatha is delivered subcutaneously.

The U.S. Wholesale Acquisition Cost (WAC) price of Repatha is \$14,100 annually, whether it is delivered monthly via *Pushtronex* system or every two weeks via SureClick® autoinjector. Actual costs to patients, payers and health systems are anticipated to be lower as WAC pricing does not reflect discounts or rebates. Out-of-pocket costs to patients will vary depending on insurance status and eligibility for patient assistance. The *Pushtronex* system will be available to patients in the U.S. in early August.

Elevated LDL-C is an abnormality of cholesterol and/or fats in the blood and is recognized as a major risk factor for cardiovascular disease.<sup>2-5</sup> In the U.S., there are approximately 11 million people with ASCVD and/or familial hypercholesterolemia (FH) who have uncontrolled levels of LDL-C over 70 mg/dL, despite treatment with statins or other cholesterol-lowering therapies.<sup>6,7</sup> FH is caused by genetic mutations that lead to high levels of LDL-C at an early age.<sup>8</sup> It is estimated that one million people in the U.S. have FH, yet less than one percent are diagnosed.<sup>9</sup>

## About Repatha® (evolocumab)

Repatha® (evolocumab) is a human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9). Repatha binds to PCSK9 and inhibits circulating PCSK9 from binding to the low-density lipoprotein (LDL) receptor (LDLR), preventing PCSK9-mediated LDLR degradation and permitting LDLR to recycle back to the liver cell surface. By inhibiting the binding of PCSK9 to LDLR, Repatha increases the number of LDLRs available to clear LDL from the blood, thereby lowering LDL-C levels.<sup>1</sup>

GLAGOV, the intravascular ultrasound study, is underway to determine the effect of Repatha on coronary atherosclerosis in approximately 950 patients undergoing cardiac catheterization to test the hypothesis of robust LDL-C reduction leading to a reduction or a change in the build-up of plaque in the arteries. Results from the GLAGOV study are expected in the second half of 2016.

The FOURIER outcomes trial is designed to evaluate whether treatment with Repatha in combination with statin therapy, compared to placebo plus statin therapy, reduces the risk of cardiovascular events in patients with high cholesterol and clinically evident cardiovascular disease, and completed patient enrollment in June 2015. Top-line results from the approximately 27,500-patient event-driven FOURIER study are anticipated in first quarter of 2017.

Repatha is approved in 43 countries, including the U.S., Japan, Canada and in all 28 countries that are members of the European Union. Applications in other countries are pending.

## Important U.S. Product Information

Repatha® is indicated as an adjunct to diet and:

- Maximally tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C)
- 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 effect of Repatha® on cardiovascular morbidity and mortality has not been determined.

The safety and effectiveness of Repatha® have not been established in pediatric patients with HoFH who are younger than 13 years old.

The safety and effectiveness of Repatha® have not been established in pediatric patients with primary hyperlipidemia or HeFH.

## Important 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% of Repatha®-treated patients and more common than placebo) 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% of Repatha®-treated patients and 1% 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% versus 0% 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% and 3.0% 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% and 0%, respectively.

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

Neurocognitive events were reported in less than or equal to 0.2% in Repatha®-treated and placebo-treated patients.

In a pool of placebo- and active-controlled trials, as well as open-label extension studies that followed them, a total of 1,988 patients treated with Repatha® had at least one LDL-C value <25 mg/dL. Changes to background lipid-altering therapy were not made in response to low LDL-C values, and Repatha® dosing was not modified or interrupted on this basis. Although adverse consequences of very low LDL-C were not identified in these trials, the long-term effects of very low levels of LDL-C induced by Repatha® are unknown.

Musculoskeletal adverse reactions were reported in 14.3% of Repatha®-treated patients and 12.8% of placebo-treated patients. The most common adverse reactions that occurred at a rate greater than placebo were back pain (3.2% versus 2.9% for Repatha® and placebo, respectively), arthralgia (2.3% versus 2.2%), and myalgia (2.0% versus 1.8%).

**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%) Repatha<sup>®</sup>-treated patients and more frequently than in placebo-treated patients, included upper respiratory tract infection (9.1% versus 6.3%), influenza (9.1% versus 0%), gastroenteritis (6.1% versus 0%), and nasopharyngitis (6.1% versus 0%).

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

Please contact Amgen Medinfo at 800-77-AMGEN (800-772-6436) or 844-REPATHA (844-737-2842) regarding Repatha<sup>®</sup> availability or find more information, including full Prescribing Information, at [www.amgen.com](http://www.amgen.com) and [www.Repatha.com](http://www.Repatha.com).

### **About Amgen 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>10</sup> Amgen's research into cardiovascular disease, and potential treatment options, is part of a growing competency at Amgen that utilizes human genetics to identify and validate certain drug targets. Through its own research and development efforts, as well as partnerships, Amgen is building a robust cardiovascular portfolio consisting of several approved and investigational molecules in an effort to address a number of today's important unmet patient needs, such as high cholesterol and heart failure.

### **About Amgen**

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its 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.

For more information, visit [www.amgen.com](http://www.amgen.com) and follow us on [www.twitter.com/amgen](https://www.twitter.com/amgen).

### **Forward-Looking Statements**

This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including 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. 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 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. 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. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. 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. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all. We are increasingly dependent on information technology systems, infrastructure and data security. 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.

The scientific information discussed in this news release relating to new indications is preliminary and investigative and is not part of the labeling

approved by the U.S. Food and Drug Administration or European Commission 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.

CONTACT: Amgen, Thousand Oaks  
Kristen Davis: 805-447-3008 (media)  
Kristen Neese: 805-313-8267 (media)  
Arvind Sood: 805-447-1060 (investors)

#### References

1. Repatha® U.S. Prescribing Information. Amgen.
2. World Health Organization. Quantifying Selected Major Risks to Health. In: The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva. 2002:49-97.
3. Merck Manuals website. [http://www.merckmanuals.com/professional/endocrine\\_and\\_metabolic\\_disorders/lipid\\_disorders/dyslipidemia.html](http://www.merckmanuals.com/professional/endocrine_and_metabolic_disorders/lipid_disorders/dyslipidemia.html). Accessed May 2016.
4. American Heart Association (2014). Why Cholesterol Matters. [http://www.heart.org/HEARTORG/Conditions/Cholesterol/WhyCholesterolMatters/Why-Cholesterol-Matters\\_UCM\\_001212\\_Article.jsp](http://www.heart.org/HEARTORG/Conditions/Cholesterol/WhyCholesterolMatters/Why-Cholesterol-Matters_UCM_001212_Article.jsp). Accessed May 2016.
5. World Health Organization. Global Status Report on Noncommunicable Diseases 2014. Geneva, 2014.
6. Amgen Data on File.
7. Centers for Disease Control and Prevention. Vital signs: prevalence, treatment, and control of high levels of low-density lipoprotein cholesterol. United States, 1999–2002 and 2005–2008. MMWR. 2011;60(4):109–14.
8. National Human Genome Research Institute. Learning About Familial Hypercholesterolemia. <http://www.genome.gov/25520184>. Accessed May 2016.
9. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial Hypercholesterolaemia is Underdiagnosed and Undertreated in the General Population: Guidance for Clinicians to Prevent Coronary Heart Disease. *Eur Heart J*. 2013;34:3478-3490.
10. World Health Organization. Cardiovascular diseases (CVDs) fact sheet. <http://www.who.int/mediacentre/factsheets/fs317/en/>. Accessed May 2016.

The Amgen logo consists of the word "AMGEN" in a bold, blue, sans-serif font. A registered trademark symbol (®) is located at the top right of the letter "N".

Photo - <http://photos.prnewswire.com/prnh/20160708/387670>

Logo - <http://photos.prnewswire.com/prnh/20081015/AMGENLOGO>

To view the original version on PR Newswire, visit: <http://www.prnewswire.com/news-releases/fda-approves-first-and-only-single-monthly-injection-for-a-pcsk9-inhibitor-300296280.html>

SOURCE Amgen