

## **News Release**

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# **REPATHA<sup>®</sup> (EVOLOCUMAB) APPROVED AS FIRST PCSK9 INHIBITOR IN JAPAN FOR THE TREATMENT OF HIGH CHOLESTEROL**

## **Important Milestone for Certain Japanese Patients With Uncontrolled LDL Cholesterol**

### **First Approval for Amgen and Astellas Joint Venture**

TOKYO (Jan. 22, 2016) – Amgen Astellas BioPharma K.K. (Headquarters, Tokyo; General Manager and Representative Director: Eiichi Takahashi, “Amgen Astellas”) and Astellas Pharma Inc. (Headquarters, Tokyo; President and CEO: Yoshihiko Hatanaka, “Astellas”) today announced that Amgen Astellas received approval for the cholesterol-lowering medication Repatha<sup>®</sup> (evolocumab) Injection, the first proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor in Japan from the Japanese Ministry of Health, Labour and Welfare. Repatha is a human monoclonal antibody that inhibits PCSK9, a protein that reduces the liver's ability to remove low-density lipoprotein cholesterol (LDL-C), or “bad” cholesterol, from the blood.<sup>1</sup>

Repatha is indicated for the treatment of patients with familial hypercholesterolemia (FH) or hypercholesterolemia who have high risk of cardiovascular events and do not adequately respond to HMG-CoA reductase inhibitors (statins).

“This approval is significant for patients and physicians in Japan and is a testament to the ongoing collaboration between Amgen and Astellas,” said Eiichi Takahashi, general manager, Amgen Astellas. “We are proud of the progress we are making toward our common goal of addressing the critical needs of Japanese patients with high LDL cholesterol who struggle to control their condition.”

Results from Phase 3 studies showed that adding Repatha to background lipid-lowering therapy that included statins resulted in intensive reductions in LDL-C. YUKAWA-2, a pivotal Phase 3 study in Japanese patients with high cardiovascular risk and high cholesterol, demonstrated that subcutaneous Repatha 140 mg every two weeks or 420 mg every four weeks, compared to placebo, in combination with daily doses of atorvastatin, reduced LDL-C by 67 to 76 percent from baseline at week 12 and at the mean of weeks 10 and 12.<sup>2</sup> The adverse events that occurred in greater than 2 percent of the Repatha group were nasopharyngitis (16.8 percent Repatha; 17.8 percent placebo), gastroenteritis (3.0 percent Repatha; 1.0 percent placebo) and pharyngitis (2.5 percent Repatha; 2.5 percent placebo).<sup>3</sup> Results from TAUSSIG, a global, open label, single-arm study in patients with homozygous FH, including patients in Japan, showed

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Repatha reduced LDL-C by approximately 23 percent.<sup>4</sup> The adverse events that occurred in greater than 5 percent of the Repatha group were nasopharyngitis (9.0 percent), and influenza (7.0 percent).<sup>4</sup>

“In Japan, LDL cholesterol levels are not adequately controlled for many patients who are at high risk of cardiovascular events and taking statins, nearly half of whom have not reached their desired LDL cholesterol goal,” said Tamio Teramoto, M.D., Ph.D., director of Teikyo Academic Research Center and investigator for the Phase 2 YUKAWA-1 trial. “As the first in a new class of medicines in Japan, Repatha offers physicians an important treatment option for patients who require additional LDL cholesterol reduction.”

Elevated LDL-C is an abnormality of cholesterol and/or fats in the blood.<sup>5,6</sup> Familial hypercholesterolemia (FH) is an inherited condition caused by genetic mutations which lead to high levels of LDL-C at an early age,<sup>7</sup> and it is estimated that less than 1 percent of people with FH in Japan are diagnosed.<sup>8</sup> Patients can have either one of two types of FH.<sup>7</sup> Heterozygous FH is the more common type of FH and in Japan, occurs in approximately one in 500 individuals.<sup>8,9</sup> It can cause LDL-C levels twice as high as normal (e.g., >180 mg/dL).<sup>9,10</sup> Individuals with heterozygous FH have one altered copy of a cholesterol-regulating gene.<sup>7</sup> Homozygous FH is a rare, more severe form.<sup>7</sup> One hundred sixty-six homozygous FH patients were diagnosed and registered as recipients of designated disease treatment in Japan as of 2014.<sup>7,11</sup> It can cause LDL-C levels more than six times as high as normal (e.g., 500-1,000 mg/dL).<sup>7,10</sup> Individuals with homozygous FH have two altered copies of cholesterol-regulating genes (one from each parent).<sup>7</sup>

Repatha is also approved in the European Union, United States and Canada.

## About Repatha® (evolocumab)

Repatha® (evolocumab) is a human monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9).<sup>1</sup> 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>2</sup>

## Indications:

Repatha is indicated for the treatment of patients with familial hypercholesterolemia (FH) or hypercholesterolemia who have high cardiovascular event risk and do not adequately respond to HMG-CoA reductase inhibitors.

## Precautions Related to Indications:

- (1) Prior to evolocumab therapy, patients should have a confirmed diagnosis of familial hypercholesterolemia or hypercholesterolemia by going through assessment.
- (2) When applying evolocumab to patients with non-familial hypercholesterolemia, it should be carefully considered for patients who have high risk of cardiovascular events based on risk factors e.g. comorbid conditions including coronary artery disease, non-cardiogenic stroke, peripheral arterial disease, diabetes and chronic renal disease or medical history.

## Dosage and Administration

Heterozygous Familial Hypercholesterolemia and Hypercholesterolemia:

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For adults, recommend Repatha (genetical recombination) of 140 mg is administrated every 2 weeks or Repatha of 420 mg is administrated every 4 weeks subcutaneously

Homozygous Familial Hypercholesterolemia:

For adults, recommend Repatha (genetical recombination) of 420 mg is administrated every 4 weeks subcutaneously. Repatha of 420 mg every 2 weeks can be administered when the efficacy is not adequate. If Repatha is administered as adjunctive therapy for patients with LDL apheresis, as starting dose, Repatha of 420 mg every 2 weeks can be administered subcutaneously

### **Precautions Related to Dosage and Administration:**

Evolocumab should be administered as an adjunct to HMG-CoA reductase inhibitor therapy [Efficacy and safety of evolocumab monotherapy in Japanese patients not confirmed.]

\* For more information, please see the latest Japan Prescribing Information.

### **About Amgen Astellas BioPharma K.K.**

Amgen Astellas BioPharma K.K. is a Japanese company that began operations on October 1, 2013, to provide breakthrough-science-based medicines to help address unmet medical needs of patients in Japan. The company is a joint venture between Amgen, one of the world's leading independent biotechnology companies, and Astellas Pharma Inc., a leading Tokyo-based R&D oriented global pharmaceutical company. The joint venture will become a wholly-owned Amgen affiliate as soon as 2020. Amgen Astellas leverages the capabilities of both companies – Amgen's science and pipeline candidates coupled with Astellas' deep knowledge of Japanese patient and physician needs, long-term commercial and regulatory experience, and strong presence as a leading company in Japan – to contribute to the creation of a healthy society.

Amgen Astellas has grown into an organization equipped with comprehensive functions to be fully operational as a marketing authorization holder. The total number of employees today exceeds 300, including its sales organization in 19 regional sales offices located across Japan. Products will be copromoted with Astellas.

### **About Astellas**

Astellas Pharma Inc., based in Tokyo, Japan, is a company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. We focus on Urology, Oncology, Immunology, Nephrology and Neuroscience as prioritized therapeutic areas while advancing new therapeutic areas and discovery research leveraging new technologies/modalities. We are also creating new value by combining internal capabilities and external expertise in the medical/healthcare business. Astellas is on the forefront of healthcare change to turn innovative science into value for patients. For more information, please visit our website at [www.astellas.com/en](http://www.astellas.com/en).

### **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.

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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 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](http://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 Inc. and its subsidiaries (Amgen 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 Jan. 22, 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,

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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 Amgen and its partners routinely obtain patents for 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 their ability to pay a dividend or repurchase our common stock.

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