

News Release

THE RESULTS FROM A ONE YEAR TREATMENT OF REPATHA PRESENTED AT THE ANNUAL MEETING OF THE JAPAN DIABETES SOCIETY (JDS 2016)

SUSTAINED EFFICACY AND GLYCEMIC SAFETY DEMONSTRATED REGARDLESS OF BASELINE GLYCEMIC STATUS

TOKYO (May 23, 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”) announced results from a one-year analysis of treatment with the cholesterol-lowering medication Repatha[®] Injection (generic name: Evolocumab (Genetically Recombination)) in Japanese hypercholesterolemia patients with Type 2 diabetes. These results were presented at the 59th Annual Meeting of the Japan Diabetes Society (JDS 2016) held in Kyoto on May 21.

The analysis demonstrated that in Japanese patients at high cardiovascular event risk with hypercholesterolemia on stable statin therapy, Repatha showed sustained efficacy and no concerning effects on glycemic control, regardless of baseline glycemic status

Lead author Director Shizuya Yamashita, Rinku General Medical Center, and Professor of Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine said, “To help prevent cardiovascular events in diabetes patients, it is important to exercise comprehensive control over risk factors for hyperlipidemia and other arteriosclerotic diseases in addition to glycemic control. This time, we were able to confirm that the new LDL-cholesterol-lowering medication Repatha demonstrated stable efficacy and safety for Japanese hypercholesterolemia patients with diabetes or who are at risk for diabetes. This knowledge is suggestive with regard to how therapy for diabetes patients whose LDL cholesterol level must be reduced more stringently should be provided in the future.”

The subjects of this sub-population analysis include 556 Japanese patients with hypercholesterolemia from the YUKAWA 1 and 2 (Study of LDL-Cholesterol Reduction Using a Monoclonal PCSK9 Antibody in Japanese Patients With Advanced Cardiovascular Risk)^{1,2} who were enrolled in the open-label extension studies OSLER 1 and 2 (Open Label Study of Long Term Evaluation Against LDL-C Trial)^{3,4} to evaluate the long-term safety and efficacy of treatment with Repatha .

The OSLER subjects were randomized to one year of open-label Repatha plus standard of care (SOC) or SOC alone. They were grouped by baseline glycemic status — Type 2 diabetes mellitus (T2DM), metabolic syndrome (MetS), or neither. In OSLER-1, mean (SE) percent changes in LDL-C at one year were –67% (2%;T2DM), –72% (3%;MetS), and –67% (2%;neither); respective changes for SOC alone were –3% (4%), 3% (4%), and –0.8% (2%). In OSLER-2, mean (SE) percent changes in LDL-C in evolocumab-

treated patients were –65% (3%;T2DM), –66% (7%;MetS), and –66% (3%;neither); respective changes for SOC alone were 26% (6%), 12% (4%), and 14% (4%).

In patients on Repatha, mean (SE) changes from baseline at one year in glucose(mg/dL) were 0.4 (3.8) for T2DM, 0.5 (1.6) for MetS, and 5.2 (1.6) for neither; respective changes for SOC alone were –6.7 (7.2), –0.4 (7.7) and 3.1 (1.6). In patients on Repatha, mean (SE) changes from baseline at one year in HbA1c were 0.07% (0.10%;T2DM), –0.08% (0.04%;MetS), and 0.08% (0.07%;neither); for SOC alone, changes were 0.02% (0.12%), 0.10% (0.15%) and –0.06% (0.02%). Overall, incidences of adverse events were 75% in patients on Repatha plus SOC and 72% in patients on SOC alone. No neutralizing antibodies were detected.

Repatha was approved in Japan by the Japanese Ministry of Health, Labour and Welfare in January 2016. 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).

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

Repatha is approved in the United States, Japan, Canada, Australia, Russia, Brazil, Hong Kong, Kuwait, Switzerland, Israel and in all 28 countries that are members of the European Union as well as in Norway, Iceland and Liechtenstein. Applications in other countries are pending.

About Repatha® (evolocumab)

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

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:

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

Homozygous Familial Hypercholesterolemia:

For adults, recommend Repatha (genetical recombination) of 420 mg is administered 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.

* The official guidance of point to consideration regarding Repatha® under the coverage of National Health Insurance is issued by Medical Affairs Division of Ministry of Health, Labour and Welfare.

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.

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 and follow us on www.twitter.com/amgen.

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