

## **News Release**

---

# **AMGEN ASTELLAS AND ASTELLAS ANNOUNCE SUBMISSION OF APPLICATION FOR INVESTIGATIONAL OSTEOPOROSIS MEDICATION ROMOSUZUMAB IN JAPAN**

TOKYO (Dec. 20, 2016) – Amgen Astellas BioPharma K.K. (Headquarters, Tokyo; General Manager and Representative Director: Mark Tennyson, “Amgen Astellas”) and Astellas Pharma Inc. (Headquarters, Tokyo; President and CEO: Yoshihiko Hatanaka, “Astellas”) announced that Amgen Astellas submitted an application seeking marketing approval of romosozumab (AMG785) for the treatment of osteoporosis for those at high risk of fracture for review to the Ministry of Health, Labour and Welfare in Japan. Amgen Astellas and Astellas are co-developing romosozumab in Japan.

Osteoporosis is a major public health issue in Japan. It is estimated that nearly 9.8 million women and three million men aged 40 or older have osteoporosis.<sup>1</sup> Fractures associated with the condition may lead to impairment in mobility and interfere with activities of daily living.<sup>1</sup>

Romosozumab is an investigational monoclonal antibody that works by binding and inhibiting the activity of sclerostin, a glycoprotein secreted by osteocytes in bone, thereby increasing bone formation and decreasing bone resorption.

The Japanese New Drug Application for marketing approval for romosozumab contains data from two pivotal Phase 3 studies: the placebo-controlled **F**RActure study in postmenopausal wo**M**en with ost**E**oporosis (FRAME) including 7,180 women with postmenopausal osteoporosis, and the place**B**o-cont**R**olled study evaluating the efficacy and **D** safety of romosozumab in treatin**G** m**E**n (BRIDGE) with osteoporosis including 245 men with osteoporosis.

In the U.S. and Canada, Amgen has submitted regulatory filings for romosozumab for the treatment of osteoporosis in postmenopausal women at increased risk of fracture.

### **About Romosozumab**

Romosozumab is an investigational bone-forming monoclonal antibody and is not approved by any regulatory authority for the treatment of osteoporosis. It is designed to work by inhibiting the activity of sclerostin and has a dual effect on bone, increasing bone formation and decreasing bone resorption. Romosozumab is being studied for its potential to reduce the risk of fractures in an extensive global Phase 3 program. This program includes two large fracture trials comparing romosozumab to either placebo or active comparator in more than 10,000 postmenopausal women with osteoporosis. Amgen and UCB are co-developing romosozumab.

**AMGEN ASTELLAS AND ASTELLAS ANNOUNCE SUBMISSION OF APPLICATION FOR INVESTIGATIONAL OSTEOPOROSIS MEDICATION ROMOSUZUMAB IN JAPAN**  
**PAGE 2**

**About the FRAME study**

FRAME is a multicenter, international, randomized, double-blind, placebo-controlled, parallel-group study in postmenopausal women with osteoporosis, defined as low bone mineral density at the total hip or femoral neck. The study evaluated the effectiveness of romosozumab treatment, compared with placebo, in reducing the risk of new vertebral fractures through 12 months. The study also further evaluated if romosozumab treatment for 12 months followed by denosumab treatment for 12 months, compared with placebo followed by denosumab treatment, was effective in reducing the risk of new vertebral fractures through 24 months. In addition, clinical fracture (a composite endpoint which encompasses all symptomatic fractures, both non-vertebral and painful vertebral fractures) risk reduction, non-vertebral fracture (fractures outside of the spine, excluding sites that are not considered osteoporotic, fractures due to high trauma or pathologic fractures) risk reduction and other endpoints were assessed at 12 and 24 months.

7,180 patients were randomized 1:1 to receive either 210 mg romosozumab subcutaneous (SC) monthly (QM) or placebo SC QM for the 12-month double-blind study period. After the placebo-controlled study period, patients entered the open-label phase where all patients received 60 mg denosumab SC every six months (Q6M) for 12 months, while remaining blinded to initial treatment. An additional 12 month extension period of open-label 60 mg denosumab SC Q6M is currently ongoing.

**About the BRIDGE study**

BRIDGE is a multi-center, international, randomized, double-blind, placebo-controlled study in men aged 55-90 years with a lumbar spine, total hip or femoral neck BMD T score  $\leq -2.5$  or  $\leq -1.5$  and a history of fragility non-vertebral fracture (excluding hip fracture) or vertebral fracture. The study evaluated the effectiveness of romosozumab treatment for 12 months, compared with placebo, in increasing BMD at the lumbar spine, as well as the effect on BMD at the femoral neck and total hip at 12 months and at six months, and the percent change from baseline in the serum bone turnover markers P1NP and CTX.

245 men with osteoporosis (163 romosozumab, 82 placebo) were randomized 2:1 to receive either 210 mg romosozumab or placebo subcutaneously once monthly for 12 months.

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

Amgen Astellas BioPharma K.K. (AABP) 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.

AABP has grown into an organization with over 300 employees and comprehensive functions to be fully operational as a marketing authorization holder in Japan. AABP's sales organization, with 19 regional sales offices located throughout Japan, will co-promote its products with Astellas. The joint venture will become a wholly-owned Amgen affiliate as soon as 2020.

## **AMGEN ASTELLAS AND ASTELLAS ANNOUNCE SUBMISSION OF APPLICATION FOR INVESTIGATIONAL OSTEOPOROSIS MEDICATION ROMOSUZUMAB IN JAPAN**

### **PAGE 3**

#### **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).

#### **Forward-Looking Statements – Amgen**

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 its 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 Amgen projects. 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 Amgen to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expects similar variability in the future. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints Amgen has selected. Amgen develops 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 Amgen may have believed at the time of entering into such relationship. Also, Amgen or others could identify safety, side effects or manufacturing problems with its products after they are on the market.

Amgen's results may be affected by its 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 its products and global economic conditions. In addition, sales of Amgen's 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

**AMGEN ASTELLAS AND ASTELLAS ANNOUNCE SUBMISSION OF APPLICATION FOR INVESTIGATIONAL OSTEOPOROSIS MEDICATION ROMOSUZUMAB IN JAPAN**  
**PAGE 4**

and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, Amgen's research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Amgen or others could identify safety, side effects or manufacturing problems with its products after they are on the market. Amgen's business may be impacted by government investigations, litigation and product liability claims. In addition, Amgen's business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If Amgen fails to meet the compliance obligations in the corporate integrity agreement between it and the U.S. government, Amgen could become subject to significant sanctions. Further, while Amgen routinely obtains patents for its products and technology, the protection offered by its patents and patent applications may be challenged, invalidated or circumvented by its competitors, or Amgen may fail to prevail in present and future intellectual property litigation. Amgen performs a substantial amount of its commercial manufacturing activities at a few key manufacturing facilities and also depends on third parties for a portion of its manufacturing activities, and limits on supply may constrain sales of certain of its current products and product candidate development. In addition, Amgen competes with other companies with respect to many of its marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for Amgen's products are supplied by sole third-party suppliers. The discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on its business and results of operations. Amgen's efforts to acquire other companies or products and to integrate the operations of companies Amgen has acquired may not be successful. Amgen may not be able to access the capital and credit markets on terms that are favorable to it, or at all. Amgen is increasingly dependent on information technology systems, infrastructure and data security. Amgen's stock price may be volatile and may be affected by a number of events. Amgen's business performance could affect or limit the ability of the Amgen Board of Directors to declare a dividend or its ability to pay a dividend or repurchase its common stock.

The scientific information discussed in this news release relating to new indications for Amgen's products is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration 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.

**AMGEN ASTELLAS AND ASTELLAS ANNOUNCE SUBMISSION OF APPLICATION FOR INVESTIGATIONAL OSTEOPOROSIS MEDICATION ROMOSUZUMAB IN JAPAN**  
**PAGE 5**

**Cautionary Notes – Astellas**

In this press release, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties.

Information about pharmaceutical products (including products currently in development) which is included in this press release is not intended to constitute an advertisement or medical advice.

###

**CONTACT:**

Amgen Astellas BioPharma K.K. Corporate Affairs, +81-3-5293-9694  
Astellas Pharma Inc. Corporate Communications, +81-3-3244-3201

**References**

1. Orimo H, Nakamura T, Hosoi T, Iki M, Uenishi K, Endo N, et al. Japanese 2011 guidelines for prevention and treatment of osteoporosis—executive summary. *Arch Osteoporos*. 2012;7:3–20. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3517709>. Accessed November 11, 2016.