Amgen Announces Approval Of Aimovig® (Erenumab) In Japan For The Suppression Of Onset Of Migraine Attacks In Adults

June 23, 2021

Migraine is a Disabling Neurological Disease that Affects More Than 8.4 Million People in Japan[1],[2]
Aimovig is the First and Only Approved Treatment in Japan to Block the Calcitonin Gene-Related Peptide Receptor (CGRP-R) That Plays an Important Role in Migraine[3]
Aimovig Continues to be the Most Utilized Anti-CGRP Pathway Therapy, With More Than Half a Million Patients Prescribed Worldwide[4]

THOUSAND OAKS, Calif., June 23, 2021 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the Japanese Ministry of Health, Labour and Welfare has granted marketing approval for Aimovig® (erenumab) for the suppression of onset of migraine attacks in adults. Aimovig is the first and only approved treatment in Japan to block the calcitonin gene-related peptide receptor (CGRP-R), which is believed to play a critical role in migraine.[3] This is also the first independent submission and approval for Amgen K.K., a wholly owned affiliate of Amgen Inc. headquartered in Tokyo.

"Today's approval further strengthens Amgen's commitment to the migraine community, and we continue to look for ways to expand the availability of Aimovig to help more patients," said Murdo Gordon, executive vice president of Global Commercial Operations at Amgen. "We've seen how much Aimovig has already helped many people living with migraine around the world. Having this treatment approved in Japan will enable us to ultimately serve more patients and help them find the right treatment for this disabling, neurological disease."

Aimovig's approval in Japan is based on results from a Phase II study (20120309) evaluating the safety and efficacy of Aimovig in adult Japanese patients with episodic migraine, and a Phase III study (20170609) evaluating the efficacy and safety of Aimovig in adult Japanese patients with episodic and chronic migraine. In both studies, Aimovig significantly reduced monthly migraine days (MMD) from baseline over months 4, 5 and 6 of the double-blind treatment period (DBTP).[5,6] The safety and tolerability of Aimovig was also consistent with previously available global data. The most commonly reported adverse reactions include constipation, injection site reactions and somnolence at an incidence of 1% or more.[5,6]

"We were impressed by the Japanese Phase III study (20170609) that showed patients treated with Aimovig saw a reduction from baseline in their monthly migraine days," said Koichi Hirata, M.D., vice president, Dokkyo Medical University. "We believe Aimovig will bring renewed hope to patients by enabling fewer monthly migraine days, and that it will become one of the preferred treatments given its long-term safety and efficacy data."

Migraine is a debilitating neurological condition and can have significant impact on many areas of a person's life.[1,7] Although approximately 8.4 million people in Japan suffer from migraine, most tend to try and endure the symptoms without seeking help from medical professionals.[2,8] In Japan, more than 70% of patients with migraine have never visited a hospital to treat their disease, and about 50% of patients try to treat their disease on their own with over-the-counter medications.[8]

"Migraine is a serious neurological disease, yet is poorly understood in Japan as a condition that requires proper treatment," said Steve Sugino, general manager, Amgen K.K. "We want patients to know they don't need to push through this disease alone. If properly treated with a therapy like Aimovig that has proven efficacy and has an established tolerability profile, they may be able to take on day-to-day tasks and challenges they had previously been forced to give up."

Aimovig (erenumab-aooe) was approved as a preventive treatment for migraine in adults in the United States on May 17, 2018. As of May 2021, it has been approved in 71 countries or territories, including the European Union, the United Kingdom, Canada, and Australia, and is approved by many regulatory authorities worldwide. In Japan, Aimovig will be administered subcutaneously in a clinical setting at a dose of one injection every four weeks, consistently from first dose to continuous administration, and likewise after resuming from interruption.

Amgen K.K. became a wholly owned affiliate of Amgen Inc. in the U.S. in April 2020. It has been co-developing and marketing products in the cardiovascular, oncology, bone, inflammation, neuroscience, and other disease areas, with Aimovig becoming its first independently developed product for patients in Japan.

About the 20120309 Study
The 20120309 study is a Phase II, randomized, placebo-controlled study comprised of a six-month (24 weeks) DBTP that evaluated the safety and efficacy of erenumab for the prevention of episodic migraine in adult Japanese patients. Participants were randomized to receive subcutaneous administration of placebo or erenumab 28 mg, 70 mg or 140 mg once every four weeks for six months. The primary endpoint was the change from baseline in mean MMD over months 4, 5, and 6 of the DBTP.[5]

About the 20170609 Study
The 20170609 study is a Phase III, randomized, placebo-controlled study comprised of a six-month (24 weeks) DBTP that evaluated the safety and efficacy of erenumab for migraine prevention in adult Japanese patients with episodic or chronic migraine. There were 261 participants randomized with a 1:1 allocation to receive subcutaneous administration of placebo or erenumab 70 mg once every four weeks. The primary endpoint was the change from baseline in mean MMD over months 4, 5, and 6 of the DBTP. Secondary endpoints were the proportion of participants with at least a 50% reduction in MMD and the change from baseline in mean monthly acute migraine-specific medication treatment days over months 4, 5, and 6 of the DBTP.[6]

About Migraine
People with frequent migraine attacks may lose more than half their life to migraine.[9,10] One attack could last longer than three days.[9] They endure debilitating pain, physical impairment, and live in constant dread of the next attack – all of which is compounded by a widespread misperception of the disease.[1,11] The 2019 Global Burden of Disease Study ranks migraine among the top 10 causes of years lived with disability worldwide.[12] Migraine is

associated with personal and societal burdens of pain, disability and financial cost, and it remains under-recognized and under-treated.[7,13]

IMPORTANT JAPAN PRODUCT INFORMATION

Product name:	Aimovig® 70 mg solution for subcutaneous injection in pen
Generic name:	Erenumab (genetical recombination),
Indication:	Suppression of onset of migraine attacks
Warnings and precautions related to indication:	• When considering the use of this drug, a thorough medical examination should be conducted to confirm that the patient is experiencing migraine episodes with or without aura more than once a month, or that the patient has chronic migraine. • This product should only be administered to patients who are experiencing difficulties in their daily lives despite non-drug therapy, appropriate acute treatment for migraine attacks, with reference to the latest guidelines etc.
Dosage:	The usual adult dosage of erenumab (genetical recombination) is 70 mg subcutaneously once every 4 weeks.

About Aimovig in the U.S.
Aimovig (erenumab-aooe) is the first FDA-approved migraine preventive treatment that targets the calcitonin gene-related peptide (CGRP) receptor, which is associated with migraine.[3,14] Aimovig has been studied in several large, global, randomized, double-blind, placebo-controlled studies to assess its efficacy and safety in migraine prevention.[15,16] Aimovig is self-administered once monthly via the easy-to-use SureClick® autoinjector, without a required loading dose.[14,17] More than 3,000 patients participated in registrational trials of Aimovig across four placebo-controlled Phase 2 and Phase 3 clinical studies and their open-label extensions.[15,16,18 - 20]

Aimovig is also being evaluated through CATALYST, a comprehensive evidence generation program initiated by Amgen and Novartis that includes over 7,500 patients across ongoing clinical trials and a robust assessment of real-world evidence. Spanning over 39 countries globally, CATALYST clinical trials will explore the role of Aimovig in comparative studies, assessing impact on novel migraine outcomes, understanding predictive biomarkers and investigating Aimovig's use in additional study populations. To date, more than 450,000 patients in the United States and 500,000 patients worldwide have been prescribed Aimovig for the preventive treatment of migraine in adults.[4,21]

IMPORTANT SAFETY INFORMATION REGARDING AIMOVIG U.S. INDICATION
Aimovig® (erenumab-aooe) is indicated for the preventive treatment of migraine in adults.

Contraindication: Aimovig® is contraindicated in patients with serious hypersensitivity to erenumab-aooe or to any of the excipients. Reactions have included anaphylaxis and angioedema.

Hypersensitivity Reactions: Hypersensitivity reactions, including rash, angioedema, and anaphylaxis, have been reported with Aimovig® in post marketing experience. Most reactions were not serious and occurred within hours of administration, although some occurred more than one week after administration. If a serious or severe reaction occurs, discontinue Aimovig® and initiate appropriate therapy.

Constipation with Serious Complications: Constipation with serious complications has been reported following the use of Aimovig® in the postmarketing setting. There were cases that required hospitalization, including cases where surgery was necessary. The onset of constipation was reported after the first dose in a majority of these cases, but patients also reported later on in treatment. Aimovig® was discontinued in most reported cases. Constipation was one of the most common (up to 3%) adverse reactions reported in clinical studies.

Monitor patients treated with Aimovig® for severe constipation and manage as clinically appropriate. Concurrent use of medications associated with decreased gastrointestinal motility may increase the risk for more severe constipation and the potential for constipation-related complications.

Hypertension: Development of hypertension and worsening of pre-existing hypertension have been reported following the use of Aimovig® in the postmarketing setting. Many of the patients had pre-existing hypertension or risk factors for hypertension. There were cases requiring pharmacological treatment and, in some cases, hospitalization. Hypertension may occur at any time during treatment but was most frequently reported within seven days of dose administration. In the majority of the cases, the onset or worsening of hypertension was reported after the first dose. Aimovig® was discontinued in many of the reported cases.

Monitor patients treated with Aimovig® for new-onset hypertension, or worsening of pre-existing hypertension, and consider whether discontinuation of Aimovig® is warranted if evaluation fails to establish an alternative etiology.

Adverse Reactions: The most common adverse reactions in clinical studies (≥ 3% of Aimovig®-treated patients and more often than placebo) were injection site reactions and constipation.

Please see Aimovig® full Prescribing Information.

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.

About Amgen K.K.
Amgen K.K. is a Japanese operation of Amgen in the U.S., one of the world's leading biotechnology companies. In October 2013, the company started as Astellas Amgen BioPharma, a joint company with Astellas Pharma, and on April 1, 2020, became a wholly owned subsidiary of Amgen with a new corporate name. Amgen K.K. focuses on disease areas with significant unmet medical needs, including cardiometabolic, oncological, bone,

inflammation/immune and neurological diseases. Currently, approximately 600 employees engage in activities from clinical development to sales with the mission of "To serve patients – Doing everything we can now, for the patients."

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 any statements on the outcome, benefits and synergies of collaborations, or potential collaborations, with any other company (including BeiGene, Ltd. or any collaboration to manufacture therapeutic antibodies against COVID-19), the performance of Otezla® (apremilast) (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), or the acquisition of Five Prime Therapeutics, Inc., as well as 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, effects of pandemics or other widespread health problems such as the ongoing COVID-19 pandemic on our business, outcomes, progress, or effects relating to studies of Otezla as a potential treatment for COVID-19, 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 current reports on 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, including our devices, 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. 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, including in Puerto Rico, 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. An outbreak of disease or similar public health threat, such as COVID-19, and the public and governmental effort to mitigate against the spread of such disease, could have a significant adverse effect on the supply of materials for our manufacturing activities, the distribution of our products, the commercialization of our product candidates, and our clinical trial operations, and any such events may have a material adverse effect on our product development, product sales, business and results of operations. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our commercial products. 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. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. 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 collaborate with or acquire other companies, products or technology, and to integrate the operations of companies or to support the products or technology we have acquired, may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. Our stock price is volatile and may be affected by a number of events. Global economic conditions may magnify certain risks that affect our business. 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. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

The scientific information discussed in this news release related to our product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates. Further, any scientific information discussed in this news release relating to new indications for our 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.

Note (Amgen K.K.)

Information on pharmaceutical products (including those under development) discussed in this news release is not intended to promote and advertise the products or offer medical advice.

References

1. Russo AF. Annu Rev Pharmacol Toxicol. 2015;55:533-552.
2. Sakai F, Igarashi H. Prevalence of Migraine in Japan: A Nationwide Survey. Cephalalgia. 1997;17(1):15-22.
3. Olesen J, Diener HS, Husstedt I, et al. Calcitonin gene-related peptide receptor antagonist BIBN 4096 BS for the acute treatment of migraine. N Engl J Med. 2004;350(11):1104-1110.
4. Novartis 2020 Annual Report, January 26, 2021.
5. Amgen (December 2015 – November 2020). A Safety and Efficacy Study to Evaluate AMG 334 in Migraine Prevention. Identifier NCT02630459. https://clinicaltrials.gov/ct2/show/NCT02630459
6. Takeshima, T., Sakai, F., Hirata, K, et al. Erenumab treatment for migraine prevention in Japanese patients: Efficacy and safety results from a Phase 3, randomized, double-blind, placebo-controlled study. *Headache*. June 2021.
7. Lipton R, Bigal M, Diamond M, et al. Migraine prevalence, disease burden and the need for preventive therapy. Neurology. 2007; 68(5):343-349.
8. The Japanese Headache Society. Clinical Practice Guideline for Chronic Headache. 2013; https://www.jhsnet.net/english/guideline2013.pdf.
9. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38(1):1-211.
10. Lipton R, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. Headache. 2001;41(7):1-211.
11. Rutberg S, Ohrling K. Migraine – more than a headache: Women's experiences of living with migraine. Disabil Rehabil. 2012;34(4):329-336.
12. Steiner, T.J., Stovner, L.J., Jensen, R. et al. Migraine remains second among the world's causes of disability, and first among young women: findings from GBD2019. J Headache Pain 2020.
13. Diamond S, Bigal ME, Silberstein S, et al. Patterns of diagnosis and acute and preventive treatment for migraine in the United States: results from the American Migraine Prevalence and Prevention study. Headache. 2007;47(3):355-363
14. Aimovig® (erenumab-aooe) prescribing information, Amgen, April 2020.
15. Sun H, Dodick DW, Silberstein S, et al. Safety and efficacy of AMG 334 for prevention of episodic migraine: a randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet Neurol*. 2016;15(4):382-390. doi:10.1016/S1474-4422(16)00019-3.
16. Tepper S, Ashina M, Reuter U, et al. Safety and efficacy of erenumab for preventive treatment of chronic migraine: a randomised, double-blind, placebo-controlled phase 2 trial. *Lancet Neurol*. 2017;16(6):425-434. doi:10.1016/S1474-4422(17)30083-2.
17. Mead J, Dammerman R, Rasmuseen S, et al. Patient Reported Ease-of-Use with a Disposable Autoinjector in Individuals with Migraine. *Patient Preference and Adherence.* July 2020.
18. Ashina M, Goadsby P, Reuter U, et al. Long-term efficacy and safety of erenumab in migraine prevention: Results from a 5-year, open-label treatment phase of a randomized clinical trial. *European Journal of Neurology*. January 2021.
19. Reuter U, Goadsby PJ, Lanteri-Minet M, et al. Sustained Efficacy and Safety of Erenumab in Episodic Migraine Patients Failing 2–4 Prior Preventive Treatments: 2-year Interim Results of the LIBERTY Open-Label Extension Study. Presented at the 18th Migraine Trust Virtual Symposium; October 3-9, 2020; London, U.K.
20. Wang S-J, Roxas Jr, A, Saravia B, et al. Efficacy and Safety of Erenumab in Patients with Episodic Migraine from the EMPOWER Study. Presented at the 18th Migraine Trust Virtual Symposium; October 3-9, 2020; London, U.K.
21. Data on File. Amgen, May 2021

CONTACT: Amgen, Thousand Oaks
Megan Fox, 805-447-1423 (media)
Michael Strapazon, 805-313-5553 (media)
Arvind Sood, 805-447-1060 (investors)

View original content to download multimedia:http://www.prnewswire.com/news-releases/amgen-announces-approval-of-aimovig-erenumab-in-japan-for-the-suppression-of-onset-of-migraine-attacks-in-adults-301318079.html

SOURCE Amgen