Aimovig™ (erenumab) Phase 3 STRIVE Data Published In The New England Journal Of Medicine Demonstrate Significant, Sustained Efficacy In Migraine Prevention

November 29, 2017

Patients With Episodic Migraine Taking Aimovig Reported Significant and Meaningful Benefits Over Six Months, With Reduced Monthly Migraine Days and Acute Medication Use

Fifty Percent of Patients Taking Aimovig 140 mg Had Their Migraine Days Cut by at Least Half - Nearly Three-Fold Higher Odds Compared to Placebo

Patients Taking Aimovig Reported Reduced Physical Impairment and Improved Ability to Participate in Daily Activities Based on a Novel Patient-Reported Outcomes Tool

Ninety Percent of Patients Completed the Six-Month Study; Data Reinforce the Safety and Tolerability Profile of Aimovig Consistently Seen in the Entire Clinical Program

THOUSAND OAKS, Calif., Nov. 29, 2017 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that the *New England Journal of Medicine* (NEJM) published positive results from the six-month Phase 3 STRIVE study evaluating Aimovig™ (erenumab) versus placebo for the prevention of episodic migraine (between four and 14 migraine days per month). Aimovig delivered clinically meaningful and statistically significant differences from placebo for all primary and secondary endpoints in the study. Patients taking Aimovig experienced a significant reduction in mean monthly migraine days and were significantly more likely to achieve a 50 percent or greater reduction in monthly migraine days than those taking placebo. Patients reported significant improvements on key measures assessing the impact of migraine on their lives when taking Aimovig, based on the Migraine Physical Function Impact Diary (MPFID) – a novel patient-reported outcomes instrument validated to specifically measure the impact of migraine on physical functioning. Aimovig is the first and only fully human monoclonal antibody designed to specifically block the calcitonin gene-related peptide (CGRP) receptor; CGRP plays a critical role in migraine activation.

To view the Multimedia News Release, go to: https://www.multivu.com/players/English/8004555-amgen-aimovig-erenumab-phase3-strive-study-migraines/.

"STRIVE is the first fully reported Phase 3 study of the CGRP pathway monoclonal antibodies, and it clearly shows that blocking this pathway can reduce the impact of migraine," said Peter Goadsby, M.D., Ph.D., FAHS, director, NIHR-Wellcome Trust King's Clinical Research Facility and professor of Neurology, King's College Hospital, London. "The results of STRIVE represent a real transition for migraine patients from poorly understood, repurposed treatments, to a specific migraine-designed therapy. STRIVE, as with the monoclonal antibody developments generally, represents an incredibly important step forward for migraine understanding and migraine treatment."

STRIVE enrolled 955 patients experiencing a mean baseline of 8.3 monthly migraine days, who were randomized to receive either placebo or subcutaneous Aimovig 140 mg or 70 mg once a month, for six months. Patients taking Aimovig at the higher dose experienced a significant 3.7-day reduction in monthly migraine days (3.2-day reduction with 70 mg, 1.8-day reduction with placebo; $p<0.001$ for both doses versus placebo). Fifty percent of patients taking Aimovig 140 mg had their migraine days cut by 50 percent or greater, representing a significantly higher likelihood of achieving this response compared to placebo (43.3 percent at 70 mg and 26.6 percent with placebo; odds ratios of 2.8 and 2.1 respectively for 140 mg and 70 mg; $p<0.001$ for both doses versus placebo). All STRIVE endpoints were assessed from baseline to the average of the last three months of the double-blind treatment phase of the study (months 4, 5, 6).

"There is a clear unmet need for efficacious, innovative therapies for the prevention of migraine. Publication of these data underscores the significance of the CGRP receptor blocker Aimovig as potentially the first available treatment targeting a pathophysiologically relevant pathway for one of the most common causes of disability across the globe," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "We look forward to advancing our robust clinical program for Aimovig in order to help ease the burden of this devastating disease and to best support the migraine patient community."

Other secondary endpoint results from the Phase 3 study include:

- Patients taking Aimovig had significant reductions in the number of days per month using an acute or "rescue" migraine-specific medication compared to those taking placebo (1.6 days with 140 mg and 1.1 days with 70 mg group, compared to 0.2-day reduction with placebo; both doses $p<0.001$ versus placebo).
- Aimovig delivered clinically meaningful benefits by reducing the impact of migraine on patients' everyday activities, such as getting ready for the day, doing household chores or activities requiring concentration (5.9 points, 140 mg; 5.5 points, 70 mg; 3.3 points, placebo; $p<0.001$ for both doses versus placebo), as measured by the MPFID instrument, validated in line with U.S. Food and Drug Administration (FDA) Patient Reported Outcomes (PRO) Guidance.[1,2] In addition, scores measuring physical impairment, such as difficulty getting out of bed or activities requiring physical effort, were also significantly reduced with Aimovig (4.8 points, 140 mg; 4.2 points, 70 mg; 2.4 points, placebo; $p<0.001$ for both groups versus placebo).[2]

In the STRIVE study, the overall safety and tolerability profiles of Aimovig were similar to that of placebo. Adverse events occurring in greater than five percent of all treatment arms were nasopharyngitis and upper respiratory tract infection. More than 90 percent of patients in the Aimovig-treated arms completed the six-month study. Adverse events leading to discontinuation of treatment occurred in 2.2 percent of patients in either Aimovig treatment arm and in 2.5 percent of patients receiving placebo. STRIVE contributes to an extensive body of evidence in support of the efficacy, safety and tolerability profile of Aimovig, including four placebo-controlled Phase 2 and Phase 3 clinical studies involving more than 2,600 patients, as well as open-label extensions up to five years in duration.

Aimovig is the first and only investigational therapy targeting the CGRP pathway to have received FDA and European Medicines Agency (EMA) regulatory filing acceptance to date. The Phase 3 STRIVE study is one of the pivotal studies included in the U.S. and European regulatory applications under review for Aimovig. If approved, Amgen and Novartis will co-commercialize Aimovig in the U.S. Amgen has exclusive commercialization rights to the drug in Japan and Novartis has exclusive rights to commercialize in rest of world.

About STRIVE

STRIVE (Study to Evaluate the Efficacy and Safety of Erenumab in Migraine Prevention, NCT02456740) is a global Phase 3, multicenter, randomized 24-week, double-blind, placebo-controlled study evaluating the safety and efficacy of Aimovig in episodic migraine (characterized in this study as ≥4 to <15 migraine days per month and <15 headache days per month on average across the three months before screening) prevention. In the study, 955 patients were randomized to receive once-monthly subcutaneous placebo, or Aimovig (70 mg or 140 mg) in a 1:1:1 ratio. Patients experienced between four and 14 migraine days each month, with an average of 8.3 migraine days per month at baseline. The primary endpoint was change in mean monthly migraine days from baseline over the last three months of the double-blind treatment phase of the study (months 4, 5 and 6). Secondary study endpoints assessed at six months included reduction of at least 50 percent from baseline in mean monthly migraine days, change from baseline in mean monthly acute migraine-specific medication days, and reductions from baseline in both mean impact on everyday activities domain and mean physical impairment domain scores on the Migraine Physical Function Impact Diary (MPFID).

About Aimovig™ (erenumab)

Aimovig is the only treatment specifically designed to prevent migraine by blocking the CGRP receptor, which is associated with migraine activation. Aimovig has been studied in several large global, randomized, double-blind, placebo-controlled studies to assess its safety and efficacy in migraine prevention. More than 2,600 patients have participated in the Aimovig clinical program across the four placebo-controlled Phase 2 and Phase 3 clinical studies and their open-label extensions. Regulatory submissions have been filed in the U.S. and Europe. The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of May 17, 2018.

About Migraine

People with frequent migraine may lose more than half their life to migraine days.[3] Migraine robs individuals of time with their families, productivity at home and at work, and their livelihoods. Migraine sufferers 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.[4] The World Health Organization ranks migraine as one of the most debilitating illnesses.[4] For the approximately 10 million Americans whose migraine frequency or severity impacts daily activities, preventive medications may be an option.[5] Approximately 3.5 million of these patients are currently on a preventive therapy, but up to 80 percent discontinue these within one year.[6,7] Migraine is associated with personal and societal burdens of pain, disability, and financial cost, and it remains under-recognized and under-treated.

About Amgen and Novartis Neuroscience Collaboration

In August 2015, Amgen entered into a global collaboration with Novartis to develop and commercialize pioneering treatments in the field of migraine and Alzheimer's disease. The collaboration focuses on investigational Amgen drugs in the migraine field, including Aimovig (Biologics License Application submitted to FDA in May 2017) and AMG 301 (currently in Phase 2 development). In April 2017, the collaboration was expanded to include co-commercialization of Aimovig in the U.S. For the migraine program, Amgen retains exclusive commercialization rights in Japan, and Novartis has exclusive commercialization rights in Europe, Canada and rest of world. Also, the companies are collaborating in the development and commercialization of a beta-secretase 1 (BACE) inhibitor program in Alzheimer's disease. The oral therapy CNP520 (currently in Phase 3 for Alzheimer's disease) is the lead molecule and further compounds from both companies' pre-clinical BACE inhibitor programs may be considered as follow-on molecules.

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.

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 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 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. 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 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 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.

*The trade name Aimovig™ is provisionally approved for use by theU.S. Food and Drug Administration.The scientific information discussed in this news release related to our product candidates ispreliminary and investigative.

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References

[1] Kawata, et al. Presented at 69th Annual Meeting of the American Academy of Neurology; April 22-28, 2017; Boston, MA.

[2] Roberts L, et al. Methods for Addressing Challenges for Evaluating Patient-Reported Outcomes in Clinical Trials of Prophylactic Treatments for Migraines. Presented at 58th Annual Meeting of the American Headache Society; June 9-12, 2016; San Diego, CA.

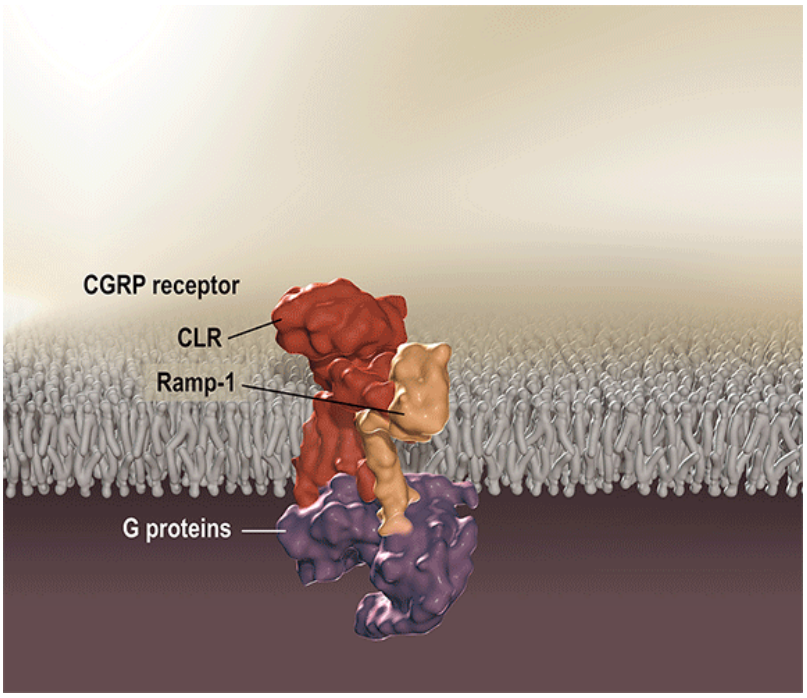
[3] Lipton RB, et al. Migraine prevalence, disease burden, and the need for preventative therapy. Neurology. 2007; 68(5):343-9.

[4] Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. JAMA. 2003;290:2443-54

[5] Headache disorders - Fact sheets. World Health Organization. http://www.who.int/mediacentre/factsheets/fs277/en/. Accessed September 17, 2017.

[6] Marketscan data on file. September 17, 2017. Ref Type: Data File

[7] Hepp Z et al. Adherence to oral migraine-preventive medications among patients with chronic migraine. Cephalalgia. 2015; 35(6):478-88.



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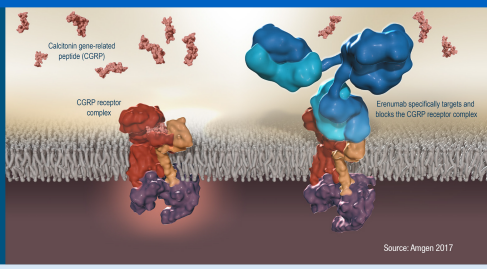
ERENUMAB*: HYPOTHESIZED MECHANISM OF ACTION

Calcitonin gene-related peptide (CGRP) is a protein that naturally exists in the body. Through its receptor, it is thought to be important in cellular signaling associated with migraine pain.[1]

Studies have shown that levels of CGRP in the body increase at the onset of migraine and return to normal following relief of migraine pain.[2,3]

Erenumab is the only fully human monoclonal antibody in late-stage development engineered to target and specifically block the CGRP receptor complex.[4,5]

*Investigational Compound



[1] Durham PL. Headache. 2006 Jun; 46(Suppl 1):53-56.
[2] Goadsby PJ et al. Ann Neurol. 1990; 28: 183-187.
[3] Goadsby PJ, Edvinsson L. Ann Neurol. 1993; 33: 48-56.
[4] Tepper et al. Lancet Neurol. 2017; 16: 425-434.
[5] ClinicalTrials.gov. https://www.clinicaltrials.gov/ct2/show/NCT02456740. Accessed October 3, 2017.

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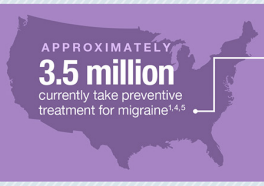
UNDERSTANDING THE BURDEN OF MIGRAINE

MIGRAINE: A SERIOUS DISEASE

Migraine is more than a headache: It is a distinct neurological disease that changes brain biology and function[1,2]

PEOPLE WITH MIGRAINE REPORT:[3]

- Painful headaches and physical impairment
- Significant disruption of daily activities
- Nausea and/or vomiting



APPROXIMATELY **3.5 million** currently take preventive treatment for migraine[1,4,5]

HOWEVER **APPROXIMATELY 70%** of patients were non-adherent to oral preventive therapy after 6 months of treatment[1,4,5]

EVERYDAY ACTIVITY IMPACT

Migraine affects not only the people living with migraine, but can also adversely impact their families due to missed activities[6]

People with migraine spend a substantial part of their lives enduring or managing around the disease[7]

ACCORDING TO THE MIGRAINE RESEARCH FOUNDATION, MORE THAN **90% OF PEOPLE** report they cannot work or function with a migraine[8]

APPROXIMATELY **$11B** is estimated to be lost by American employers each year[9]

According to the 2015 Global Burden of Disease study, migraine is one of the most debilitating of all illnesses[10]

Migraine is associated with personal and societal burdens of pain and disability, and it remains underrecognized and undertreated,

WITH APPROXIMATELY **40% GOING UNDIAGNOSED**[11]

PREVALENCE

WOMEN are three times more likely to get a migraine than men[12]

3X



MIGRAINE is most common between the ages of **30** and **39**[6]

Relatives of individuals with migraine are approximately **2 TIMES MORE LIKELY TO SUFFER** migraine than relatives of individuals who don't have migraine[13]

1 Russo AF. Calcitonin Gene-Related Peptide (CGRP): A New Target for Migraine. *Annu Rev Pharmacol Toxicol*. 2015; 55:533-552.

2 Buse DC, et al. Chronic migraine prevalence, disability, and sociodemographic factors: results from the American Migraine Prevalence and Prevention Study. *Headache*. 2012; 52(10): 1456-70.

3 Headache Classification Committee of the International Headache Society (IHS): The International Classification of Headache Disorders, 3rd Edition (beta version). *Cephalalgia*. 2013; 33 629-808.

4 Hepp Z, et al. Adherence to oral migraine-preventive medications among patients with chronic migraine. *Cephalalgia*. 2015; 35(6):478-88.

5 Marketscan data on file. 31March2017. Ref Type: Data File.

6 Lipton RB, et al. Migraine prevalence, disease burden and the need for preventative therapy. *Neurology*. 2007; 68(5):343-349.

7 Buse DC, et al. Assessing and managing all aspects of migraine: migraine attacks, migraine-related functional impairment, common comorbidities, and quality of life. *Mayo Clin Proc*. 2009; 84(5):422-435.

8 Migraine Research Foundation. Migraine Facts. Available https://migraineresearchfoundation.org/about-migraine/migraine-facts. Accessed October 2016.

9 Bonafede MM, et al. Poster presented at ISPOR 19th Annual European Congress. October 29 – November 2, 2016.

10 Global Burden of Disease Study 2013 Collaborators. *Lancet*. 2013;386:743-800.

11 Diamond 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.

12 Gasparini CF, et al. Studies on the Pathophysiology and Genetic Basis of Migraine. *Curr Genomics*. 2013; 14:300-315.

13 WF Stewart, et al. Past adult lead exposure is linked to neurodegeneration measured by brain MRI. *Neurology*. 2006; 66(3):344-348.

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FACT SHEET

Erenumab Investigational Product

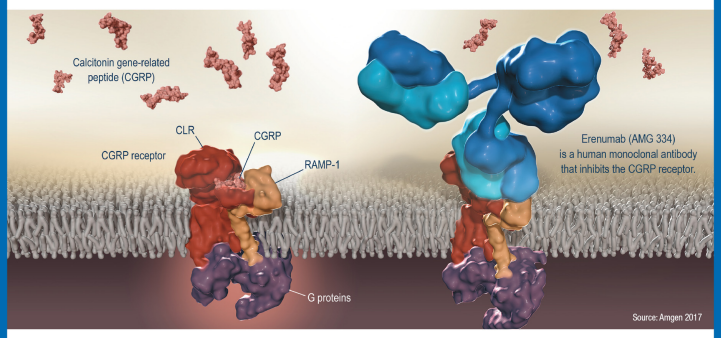
OVERVIEW

Erenumab (AMG 334) is an investigational therapy specifically designed to prevent migraine by blocking the receptor for calcitonin gene-related peptide (CGRP), which is associated with migraine activation. The U.S. Food and Drug Administration (FDA) is currently reviewing the Biologics License Application (BLA) for erenumab for the prevention of migraine in patients experiencing four or more migraine days per month. The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of May 17, 2018. Erenumab will be jointly commercialized in the U.S. by Amgen and Novartis.

THE CGRP PATHWAY

CGRP has long been thought to play a pivotal role in the pathophysiology of migraine;[1,2,3] the binding of CGRP with its receptors has been implicated in transmitting migraine pain.[1,3,4,5,6] In patients with migraine, CGRP levels increase at the onset of migraine and levels return to normal upon relief of migraine pain with triptan therapy.[7] Additionally, infusion of CGRP can induce migraine attacks in people who live with the disease.[8]

HYPOTHESIZED MECHANISM OF ACTION



Erenumab is a human (with no animal sequence) IgG2 monoclonal antibody that selectively binds to the CGRP receptor.[9]

SELECT PHASE 2 AND 3 STUDIES

Amgen has conducted a global development program to investigate the potential for erenumab (AMG 334) to help people with migraine. Click on the link below to view the study summaries on **www.clinicaltrials.gov**.

A Study to Evaluate the Efficacy and Safety of AMG 334 in Chronic Migraine Prevention (NCT02066415)

PURPOSE: Evaluate effect of AMG 334 compared to placebo on change from baseline in monthly migraine days

A Study to Assess the Long-term Safety and Efficacy of AMG 334 in Chronic Migraine Prevention (NCT02174861)

PURPOSE: Assess the long-term safety and efficacy of AMG 334

A Study to Evaluate the Efficacy and Safety of AMG 334 in Migraine Prevention (ARISE) (NCT02483585)

PURPOSE: Evaluate effect of AMG 334 compared to placebo on change from baseline in monthly migraine days in subjects with episodic migraine

A Study to Evaluate the Efficacy and Safety of AMG 334 in Migraine Prevention (STRIVE) (NCT02456740)

PURPOSE: Evaluate effect of AMG 334 compared to placebo on change from baseline in monthly migraine days in subjects with episodic migraine

Treadmill CV Safety Study (NCT02575833)

PURPOSE: Evaluate the effect of AMG 334 compared to placebo on exercise time during an exercise treadmill test in subjects with stable angina

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