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Novartis announces Phase III STRIVE data published in NEJM demonstrating significant and sustained efficacy of erenumab in migraine prevention

- *Patients with episodic migraine taking erenumab reported significant and meaningful benefits over six months, with reduced migraine days and acute medication use*

- *Fifty percent of patients taking erenumab 140mg had their migraine days cut by at least half – nearly three-fold higher odds compared to placebo*

- *Patients on erenumab reported reduced physical impairment and improved ability to participate in daily activities based on a validated patient-reported outcome tool*

- *Ninety percent of patients completed the six-month study; data reinforce placebo-like safety and tolerability profile of erenumab consistently seen in the entire clinical program*

Basel, November 29, 2017 – Novartis today announced that the New England Journal of Medicine (NEJM) published positive results from the six-month Phase III STRIVE study evaluating erenumab in the prevention of episodic migraine (defined in STRIVE as 4 to 14 migraine days per month)[1]. Erenumab delivered clinically meaningful and statistically significant differences from placebo for all primary and secondary endpoints including those measured by the novel, validated Migraine Physical Function Impact Diary (MPFID)[2]. Treatment with erenumab was well tolerated, with a safety profile comparable to placebo. Erenumab is the first and only fully human monoclonal antibody of its kind, designed to specifically block the CGRP receptor, which plays a critical role in migraine activation.

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

Principal Investigator, Peter Goadsby, M.D., Ph.D., FAHS, Director, NIHR-Wellcome Trust King's Clinical Research Facility and Professor of Neurology at King's College Hospital, London, shared his view on what the findings could mean for those with migraine, "STRIVE is the first fully reported phase III study of the CGRP pathway monoclonal antibodies, and it clearly shows that blocking this pathway can reduce the impact of migraine," Prof. Goadsby said, "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."

"The results of the STRIVE study add to the evidence for the significant, consistent benefits of erenumab seen across the spectrum of chronic and episodic migraine, including patients who failed on previous preventive treatments," said Vas Narasimhan, Global Head of Drug Development and Chief Medical Officer for Novartis. "People with migraine are missing out due to this debilitating neurological disease and are in need of safe, tolerable and effective preventive treatments. We are committed to bringing this much-needed treatment option to patients as soon as possible."

Other secondary endpoint results from the study include:

- Patients taking erenumab had significant reductions in the number of days per month using an acute or "rescue" migraine-specific medication (1.6 days for 140mg group and 1.1 days for 70mg compared to 0.2-day reduction with placebo; both $p<0.001$).
- Results from the MPFID showed erenumab delivered 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, 140mg; 5.5 points, 70 mg; 3.3 points, placebo; both $p<0.001$).
- MPFID scores in physical impairment, such as getting out of bed or activities requiring physical effort, were also significantly reduced with erenumab (4.8 points, 140mg; 4.2 points, 70 mg; 2.4 points, placebo; both $p<0.001$).

In STRIVE, more than 90% of patients taking erenumab completed the study. Adverse reactions leading to discontinuation of treatment occurred in 2.2% of erenumab-treated patients and in 2.5% of patients receiving placebo. STRIVE contributes to an extensive body of evidence in support of the efficacy, safety and tolerability profile of erenumab, including four placebo-controlled Phase II and Phase III clinical studies involving more than 2,600 patients, as well as an ongoing open-label extension up to five years in duration.

Erenumab is the first investigational therapy targeting the CGRP pathway to have received FDA and EMA regulatory filing acceptance to date. The STRIVE study is one of the pivotal trials included in the US and EU regulatory applications under review for erenumab. If approved, Novartis and Amgen will co-commercialize erenumab in the US. Amgen has exclusive commercialization rights to the drug in Japan and Novartis has exclusive rights to commercialize in rest of world.

About STRIVE

STRIVE (NCT02456740) is a global Phase III, multicenter, randomized 24-week, double-blind, placebo-controlled study evaluating the safety and efficacy of erenumab in episodic migraine (4 to 14 migraine days a month) prevention. In the study, 955 patients were randomized to receive once-monthly subcutaneous placebo, or erenumab (70mg or 140mg) 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)[3].

Secondary study endpoints assessed in the same treatment phase included the proportion of patients with a reduction of at least 50% from baseline in mean monthly migraine days, change from baseline in mean monthly acute migraine-specific medication days. The impact of migraine on physical function and the impact on everyday activities were each assessed as secondary endpoints by the Migraine Physical Function Impact Diary (MPFID), a scale developed to measure these two domains. The scale has been validated in line with US Food and Drug Administration Patient Reported Outcomes Guidance[2].

About erenumab (AMG 334)
Erenumab (AMG 334) is the only treatment specifically designed to prevent migraine by blocking the CGRP receptor, which plays an important role in migraine activation. Erenumab 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 our clinical trial program across the four placebo-controlled Phase II and Phase III clinical studies and their open-label extensions.

About Migraine
Migraine is a distinct neurological disease[4]. It involves recurrent attacks of moderate to severe head pain that is typically pulsating, often unilateral and associated with nausea, vomiting and sensitivity to light, sound and odors[5]. Migraine is associated with personal pain, disability and reduced quality of life, and financial cost to society[6]. It has a profound and limiting impact on an individual's abilities to carry out everyday tasks, and was declared by the World Health Organization to be one of the top 10 causes of years lived with disability for men and women[7]. It remains under-recognized and under-treated[6,8]. Existing preventive therapies have been repurposed from other indications[5] and are often associated with poor tolerability and lack of efficacy, with high discontinuation rates among patients[9].

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

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or manufacturing issues, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis
Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 121,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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