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Novartis presents data demonstrating efficacy of AMG 334 (erenumab) in migraine prevention at the American Headache Society Annual Meeting

- *Data from the comprehensive clinical program show AMG 334 (erenumab) is safe and effective at preventing migraine in patients with 4 or more migraine days per month*
- *AMG 334 (erenumab) significantly reduced monthly migraine days in patients with the highest need, suffering from chronic migraine with acute medication overuse*
- *Migraine patients urgently need new treatment options, as currently available preventive therapies are often discontinued due to side effects or lack of effectiveness*

Basel, June 08, 2017 – Novartis today announced that it will present 19 scientific abstracts at the 59th Annual Scientific Meeting of the American Headache Society (June 8-11, 2017, Boston, USA). This includes a new analysis from a pivotal study highlighting the efficacy of AMG 334 (erenumab) in patients with 15 or more headache days a month (chronic migraine) and a recent history of acute migraine medication overuse.[1] Also being presented at AHS are detailed results of STRIVE and ARISE, two Phase III studies of erenumab in people with 4 to 14 migraine days per month.[2,3] Erenumab is the first fully human monoclonal antibody therapy specifically designed to target and block the Calcitonin Gene-Related Peptide (CGRP) receptor, believed to play a critical role in mediating the incapacitating pain of migraine. CGRP levels rise during a migraine attack and normalize when the attack goes away.[4]

"Migraine is one of the most debilitating neurological diseases, yet it is often misunderstood or ignored, despite devastating effects on patients' personal and professional life," said Vasant Narasimhan, Global Head Drug Development and Chief Medical Officer for Novartis. "We are confident that with erenumab we are a step closer to offering a preventive therapy that is both efficacious and well-tolerated, ultimately helping patients to claim their lives back."

Excessive use of acute pain-relief medication is common among people who suffer from migraine. Many patients experience low treatment satisfaction and enter a vicious cycle as they continue to take more and more acute migraine medications, while desperately trying to control their symptoms. Forty-one percent (274) of patients in the erenumab chronic migraine trial had recent history of medication overuse. Even in these difficult to treat patients, erenumab showed significant benefits. Both doses of erenumab (70mg and 140mg) significantly reduced monthly migraine days by an average of -6.6 days from baseline. These reductions were also statistically significant ($p<0.001$ in both doses) versus placebo (-3.5 days). Furthermore, days requiring acute pain-relief drugs were also reduced in both dosage arms (by 5.4 days for 70mg; 4.9 for 140mg; 2.1 for placebo, $p <0.001$).[1]

Detailed results from the positive 6 month STRIVE study of erenumab 70mg and 140mg, and the positive 3 month ARISE study of erenumab 70mg will also be presented at the meeting. These data include both primary and secondary endpoints, evaluating the reduction in monthly migraine days and the percentage of patients who responded to erenumab. Results from STRIVE have been submitted for peer-reviewed publication.

Erenumab is currently being investigated for migraine prevention and these data support the first regulatory filing packages submitted in the United States and European Union for a CGRP inhibitor in migraine prevention. Across the four placebo-controlled Phase II and Phase III clinical studies, more than 2,600 people have been exposed to erenumab. In addition, an ongoing extension trial is underway, evaluating erenumab in people with migraine for up to 5 years.

Novartis and Amgen will co-commercialize AMG 334 (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.[5]

About the AMG 334 (erenumab) Clinical Trials Program
Erenumab has been extensively studied in several large global, randomized, double-blind, placebo-controlled trials to assess its safety and efficacy in migraine prevention in more than 2,600 people, and a 5-year extension trial is currently underway. Following the initial Phase II dose finding study, the efficacy of erenumab in migraine prevention has been shown in a Phase II trial and two Phase III trials. The safety profile of erenumab in these studies was comparable to placebo.[6,7,8]

<u>About the AMG 334 (erenumab) pivotal Phase II chronic migraine study being presented at AHS</u>
This pivotal Phase II study is a global, randomized, 12-week, double-blind, placebo-controlled study evaluating the efficacy and safety of erenumab in chronic migraine (characterized as at least 15 headache days per month, of which eight or more are migraines, for more than three months) prevention.[9] In the study, 667 patients were randomized to receive once-monthly subcutaneous placebo or erenumab 70mg or 140mg in a 3:2:2 ratio respectively.[9] Patients experienced a mean of approximately 18 migraine days per month at baseline. The primary outcome measure was the change in monthly migraine days from baseline to the last four weeks of the 12-week treatment phase in patients with chronic migraine (the number of migraine days between weeks 9 and 12).[9]

<u>About AMG 334 (erenumab) Phase III episodic migraine studies</u>
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 (characterized as up 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.[10,11] Patients experienced between four and 14 migraine days each month, with an average of 8.3 migraine days per month at baseline.[11] 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).[10,11]

The ARISE study (NCT02483585) is a global Phase III, multicenter, randomized 12-week, double-blind, placebo-controlled study evaluating the safety and efficacy of erenumab in episodic migraine prevention.[12] In the study, 577 patients were randomized to receive once-monthly subcutaneous placebo or erenumab (70mg) in a 1:1 ratio.[11,12] Patients enrolled in ARISE were experiencing between four and 14 migraine days each month.[12] The primary endpoint was change in monthly migraine days from baseline to the last four weeks of the 12-week treatment phase in patients with episodic migraine (the number of migraine days between weeks 9 and 12).[12]

About AMG 334 (erenumab)
Erenumab is a human monoclonal antibody specifically designed to target and block the Calcitonin Gene-Related Peptide (CGRP) receptor, believed to play a critical role in mediating the incapacitating pain of migraine.[13]

About Migraine
Migraine is a distinct neurological disease.[14] 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.[15] Migraine is associated with personal pain, disability and reduced quality of life, and financial cost to society.[16] 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.[17] It remains under-recognized and under-treated.[16,18] Existing preventive therapies have been repurposed from other indications and are often associated with poor tolerability and lack of efficacy, which lead to increasing discontinuation rates and dissatisfaction among patients.[19]

The cause and triggers of migraine are not fully understood as no two migraines are the same. However, Calcitonin Gene-Related Peptide (CGRP) has long been thought to play a role in the underlying pathophysiology of migraine.[20] CGRP is a molecule that binds to the CGRP receptor complex, and is thought to be responsible for transmitting the pain signals associated with migraine.[21] Levels of CGRP have been found to increase at the onset of migraine symptoms, and to return to normal when the migraine pain diminishes.[22] CGRP is also involved in vasodilation and sensory transmission which takes place during a migraine.[13]

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 and EU EMA in May 2017) and AMG 301 (currently in Phase I development). In April 2017, the collaboration was expanded to include co-commercialization of erenumab in the U.S. For the migraine program, Amgen retains sole commercialization rights in Japan, and Novartis has commercialization rights in Europe, Canada and rest of world. Also, the companies are partnering in the development and commercialization of a beta-secretase 1 (BACE) inhibitor program in AD. The oral therapy CNP520 (currently in Phase II/III for AD) is the lead molecule and further compounds from both companies' pre-clinical BACE inhibitor programs may be considered as follow-on molecules.

Novartis in Neuroscience
Novartis has a strong ongoing commitment to neuroscience (NS) and to bringing innovative treatments to patients suffering from neurological conditions where there is a high unmet need. We are committed to supporting patients and physicians in multiple disease areas, including Multiple Sclerosis (MS), Alzheimer's disease, Parkinson's disease, Epilepsy and Attention Deficit Hyperactivity Disorder, and have a promising pipeline in MS, Alzheimer's disease, migraine and specialty neurology (e.g. neuropathic pain).

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as “believed to,” “confident,” “step closer,” “will,” “being investigated,” “submitted,” “ongoing,” “underway,” "pioneering," “investigational,” "may,” “commitment,” “committed,” “pipeline,” or similar terms, or by express or implied discussions regarding potential marketing approvals for AMG 334, CNP520, AMG 301, other BACE inhibitors of Novartis and Amgen, and other investigational compounds of Novartis and Amgen subject to the collaboration, potential new indications or labeling for products in the Novartis Neuroscience portfolio, or regarding potential future revenues from such investigational compounds and products, and potential future revenues from the collaboration with Amgen. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that AMG 334, CNP520, AMG 301, other BACE inhibitors of Novartis and Amgen, or other investigational compounds of Novartis and Amgen subject to the collaboration will be submitted or approved for sale in any market, or at any particular time. Neither can there be any guarantee that the collaboration with Amgen will achieve any or all of its intended goals and objectives, or be commercially successful. Nor can there be any guarantee that any product in the Novartis Neuroscience portfolio will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Neither can there be any guarantee that AMG 334, CNP520, AMG 301, any of the other investigational compounds subject to the collaboration with Amgen, or any product in the Novartis Neuroscience portfolio will be commercially successful in the future. In particular, management’s expectations regarding such investigational compounds and products, and the collaboration with Amgen, could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; the company’s ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing and reimbursement pressures; safety, quality 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 118,000 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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