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Novartis presents new analysis demonstrating AMG 334 (erenumab) significantly reduced monthly migraine days in patients who failed previous preventive therapies

- *AMG 334 (erenumab) delivered consistent reductions in monthly migraine days for patients with chronic migraine and prior treatment failure, a population with significant unmet need*
- *Dedicated cardiovascular safety study reaffirmed placebo-like tolerability of erenumab as seen consistently across the comprehensive clinical program*
- *Erenumab is the first and only fully human monoclonal antibody of its kind, uniquely designed to specifically block the CGRP receptor, which plays a critical role in activation of migraine*

Basel, September 7, 2017 – Novartis today announced new analyses across a spectrum of patients building a clear picture of the potential of AMG 334 (erenumab) for migraine prevention. The data, being presented at the 18th Congress of the International Headache Society (IHC, Vancouver, Canada), add to the consistent efficacy and safety results to date, and also cover quality of life, burden of disease and health economic topics relating to migraine. A new analysis from a pivotal Phase II study shows erenumab reduced monthly migraine days in patients with chronic migraine for whom previous preventive treatments have failed¹. New data in a cardiovascular population with stable angina, reaffirming erenumab's safety profile, is also being presented at IHC². Erenumab is the first and only fully human monoclonal antibody designed to prevent migraine by targeting and blocking the calcitonin gene-related peptide (CGRP) receptor, believed to play a critical role in mediating the incapacitating pain of migraine.

Studies have shown that up to 80% of people with migraine discontinue preventive treatment within one year³. In a pre-specified sub-analysis from the pivotal phase II study, erenumab showed benefits even in people with chronic migraine who have tried and failed on two or more preventive treatments in the past. In these patients, erenumab cut the average number of migraine days by at least five days and up to a week per month, depending on treatment dose (70mg: -5.4 days, 140mg: -7 days, placebo: -2.7 days; p<0.001 for both doses). Furthermore, this group also had three to four times higher odds of having their migraine days cut by 50% or more compared to placebo (70 mg: 35.6 percent, 140 mg: 41.3 percent, placebo: 14.2 percent; p<0.001 for both doses versus placebo)¹.

“These data highlight that erenumab has the potential to be a life-changing option for migraine patients with the highest unmet need – those who have tried and failed previous preventive treatments,” said Professor Messoud Ashina of the Danish Headache Center and Department

of Neurology, University of Copenhagen, Denmark. “By significantly cutting migraine days, erenumab could help people get back much of their lives, which is what matters most to them”

“We are excited about erenumab’s potential to prevent migraine for many sufferers, including those for whom previous preventive treatments have been ineffective or intolerable,” said Vas Narasimhan, Global Head Drug Development and Chief Medical Officer for Novartis. “The data presented at IHC add to the extensive and ever-growing body of evidence in support of the efficacy, safety and tolerability profile of erenumab.”

Also presented at IHC are results from a safety study assessing erenumab 140 mg in a population of patients with stable angina². The study showed that erenumab had no impact on cardiovascular function, addressing questions whether targeting the CGRP pathway could have consequences for those with pre-existing heart disease. The results demonstrated that all study participants, whether given placebo or erenumab, were able to successfully complete a treadmill “stress test” (often used to gauge how well a patient’s heart can handle exercise) with no significant differences observed between the two groups. Those given erenumab showed no significant decrease in exercise time compared to those given placebo. In addition, no differences were seen between the two groups in time to onset of angina or time to onset of electrocardiogram change consistent with onset of myocardial ischemia (reduced blood flow to the heart). The treatment difference in mean change from baseline in exercise time was -11.0 seconds (90 percent confidence interval -44.9, 22.9)². Adverse events were reported by 27 percent of participants given erenumab (most common adverse events were headache and viral upper respiratory infection both 4.5 percent) and by 32 percent of participants given placebo (most common adverse events were hypotension, influenza and viral infection, all 4.5 percent). Erenumab is the only biologic anti-CGRP receptor pathway drug that has shown such supportive safety data. These results are consistent with its placebo-like safety profile, as seen across the broad clinical program involving over 2,600 migraine patients.

Erenumab is the first biologic anti-CGRP receptor drug to have received FDA and EMA regulatory filing acceptance. If approved, 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.

About the 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 five-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^{4,5,6}.

About the Erenumab pivotal Phase II chronic migraine study

The erenumab pivotal Phase II study (NCT02066415) 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) prevention⁷. In the study, 667 patients were randomized to receive once-monthly subcutaneous placebo or erenumab 70mg or 140mg in a 3:2:2 ratio respectively⁷. 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)⁷.

About the Treadmill Cardiovascular Safety Study

The erenumab treadmill cardiovascular study (NCT02575833) is a double-blind, placebo-controlled cardiovascular safety study in patients with stable angina due to documented coronary artery disease. Patients were randomized 1:1 to a single intravenous infusion of erenumab 140 mg or placebo stratified by baseline total exercise time (TET; < 7 minutes or ≥ 7 minutes) defined as the average TET of two qualifying exercise tolerance tests (ETTs) performed during screening. Following study drug administration on day 1, a post-administration ETT was conducted. The primary endpoint was the change from baseline in exercise duration as measured by TET with a non-inferiority margin of –90 seconds. Secondary efficacy endpoints included time to onset of ≥ 1 mm ST-segment depression and time to onset of exercise-induced angina during the ETT. Safety follow-up visits occurred every 2–4 weeks for 12 weeks. Adverse events were reported by 27 percent of participants given erenumab (most common adverse events were headache and viral upper respiratory infection both 4.5 percent) and by 32 percent of participants given placebo (most common adverse events were hypotension, influenza and viral infection, all 4.5 percent). These reported adverse events were consistent with the known safety profile of erenumab⁸.

About AMG 334 (erenumab)

AMG 334 (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 migraine⁹.

About Migraine

Migraine is a distinct neurological disease¹⁰. 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 odors¹¹. Migraine is associated with personal pain, disability and reduced quality of life, and financial cost to society¹². 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 women¹³. It remains under-recognized and under-treated^{12,14}. 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 patients³.

About Amgen and Novartis Neuroscience Collaboration

Since 2015, Amgen and Novartis have collaborated to jointly develop and commercialize pioneering treatments in the field of migraine and Alzheimer's disease (AD). This includes investigational Amgen drugs in the migraine field including AMG 334 (erenumab) (Biologics License Application accepted by the FDA in July 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 exclusive rights in Japan, and Novartis has exclusive rights in Europe, Canada and rest of world. The companies are also partnering in the development and commercialization of a beta-secretase 1 (BACE) inhibitor program in AD.

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This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “plan,” “expect,” “anticipate,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for AMG 334 or the other investigational or approved products described in this press release, or regarding potential future revenues from such products or the collaboration with Amgen. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations 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 or the other investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling 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 AMG 334 or the other investigational or approved products described in this press release will be commercially successful in the future. In particular, our expectations regarding such products 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; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; general economic and industry conditions, including the effects of the persistently weak economic and financial environment in many countries; 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 119,000 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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