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Novartis presents new positive data at EHMTIC showing AMG 334 significantly reduces monthly migraine days in chronic migraine

- *Detailed results from Phase II study in chronic migraine prevention showed patients on AMG 334 (erenumab) were significantly more likely to experience a 50% or more reduction in monthly migraine days compared to placebo*

- *Chronic migraine is the most disabling form of the disease, and is associated with substantial personal pain and disability, and financial cost to society*[1,2]

- *AMG 334 is being co-developed by Novartis and Amgen for the prevention of migraine*

Basel, September 15, 2016 – Novartis today announced detailed Phase II results showing the fully human monoclonal antibody AMG 334 (erenumab) demonstrated a statistically significant reduction in monthly migraine days compared with placebo in patients with chronic migraine (CM).[3] Significantly more patients receiving monthly subcutaneous AMG 334 70mg or 140mg experienced a 50% or more reduction in the number of monthly migraine days compared with placebo (40%, 41% and 24%, respectively).[3] The data are being presented at the 5th European Headache and Migraine Trust International Congress (EHMTIC) in Glasgow, Scotland.

“This is an exciting time in the treatment of chronic migraine, which has a profound impact on the lives of those who suffer from the disease,” said Vasant Narasimhan, Global Head Drug Development and Chief Medical Officer for Novartis. “These important data further support the efficacy of AMG 334 in patients who currently have limited therapeutic options. We are committed to continuing our work in migraine to provide a potential new treatment to patients suffering from this debilitating disease.”

The study included 667 patients who had a mean baseline of approximately 18 migraine days per month, and were randomized to receive either subcutaneous placebo or subcutaneous AMG 334 70mg or 140mg once a month.[4] Across both doses, patients observed a statistically significant 6.6-day reduction from baseline in monthly migraine days compared with 4.2 days observed in those on placebo ($p<0.001$).[3] A reduction of 50% or more in number of monthly migraine days was observed in 40% and 41% (70mg and 140mg doses, respectively) of individuals in the AMG 334 groups, representing a significantly higher likelihood of response compared to 24% of those receiving placebo (both $p<0.001$).[3] All endpoint assessments compared the last four weeks of the 12-week treatment phase to baseline.[4]

Other key secondary endpoints results from the Phase II CM study are:

- Reductions in monthly acute migraine-specific medication days (i.e. the number of days where patients took a migraine-specific medication in a month) were 3.5 days and 4.1 days in the 70mg and 140mg groups, respectively, representing significant reductions compared to a 1.6-day reduction in those receiving placebo (both $p<0.001$).[3]

- All groups showed numeric improvements in cumulative monthly headache hours. Compared to a 55.22-hour reduction vs. baseline in the placebo group, reductions were 64.76 hours for 70mg AMG 334 and 74.53 hours for 140mg AMG 334.[3]
- In an analysis of exploratory endpoints, both doses of AMG 334 were associated with significant improvements in health-related quality of life, headache impact, disability, and pain interference outcome measurements, compared to placebo.*[5]

The safety profile of AMG 334 was similar to placebo across both treatment arms.[3] No adverse event was reported in greater than five percent of patients treated with AMG 334. The most common adverse events (in placebo, 70mg AMG 334 and 140mg AMG 334 groups, respectively) were injection site pain (1.1%, 3.7% and 3.7%), upper respiratory tract infection (1.4%, 2.6% and 3.2%) and nausea (2.5%, 2.1% and 3.2%).[3]

Migraine is the most prevalent of all neurological disorders, with more than 10% of the worldwide population affected.[1] It profoundly limits patients' abilities to carry out everyday tasks and as such, the World Health Organization has declared migraine to be one of the top ten causes of disability for men and women.[1,6] CM is characterized by at least 15 headache days per month, of which eight or more days have migraine features, for more than three months.[7,8] It is the most debilitating form of migraine, and it is challenging for healthcare professionals to treat. As such, CM patients experience a substantial negative impact on daily activities and quality of life.[9]

Results from Phase III studies investigating AMG 334 in episodic migraine are expected later this year. AMG 334 is being co-developed by Amgen and Novartis. As part of the collaboration, Amgen retained commercialization rights in the U.S., Canada and Japan, and Novartis has rights in Europe and rest of world.

* Assessment tools for exploratory endpoints included the Headache Impact Test (HIT-6™), Migraine Disability Assessment (MIDAS), Migraine-Specific Quality-of-Life Questionnaire (MSQ), and the Patient Reported Outcome Measurement Information System (PROMIS®) Pain Interference Scale Short Form. Exploratory endpoints were not adjusted for multiple comparisons.

About the Phase II Chronic Migraine Study

The Phase II chronic migraine study is a global Phase II, randomized, 12-week, double-blind, placebo-controlled study evaluating the efficacy and safety of AMG 334 in chronic migraine prevention.[4] In the study, 667 patients were randomized to receive once-monthly subcutaneous placebo or AMG 334 (70mg or 140mg) in a 3:2:2 ratio respectively.[4] 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 nine and 12).[4] Secondary study endpoints included achievement of at least a 50% reduction from baseline in monthly migraine days in the last four weeks of the 12-week treatment phase (50% responder rate), acute migraine-specific medication use days, and change from baseline in cumulative monthly headache hours.[4] Exploratory endpoints included health-related quality of life, headache impact, disability, and pain interference outcome measurements.[4]

About Migraine

Migraine involves recurrent attacks of incapacitating head pain that is typically pulsating, often unilateral and associated with nausea, vomiting and sensitivity to light, sound and odors.[10] Migraine is associated with personal pain, disability and reduced quality of life, and financial cost to society.[2] It remains under-recognized and under-treated with more than 40% of people going undiagnosed.[2,11] Chronic migraine is characterized by at least 15 headache days per month, of which eight or more days have migraine features, for more than three months.[7,8]

About AMG 334
AMG 334 is a fully human monoclonal antibody being investigated for the prevention of migraine. AMG 334 binds to the Calcitonin-Gene-Related-Peptide (CGRP) receptor, thereby inhibiting its activation by CGRP. Through its receptor, CGRP is thought to be pivotal in the genesis of migraine.[12] AMG 334 is currently being studied in several large global, randomized, double-blind, placebo-controlled trials to assess its safety and efficacy in migraine prevention.

About the Amgen and Novartis Neuroscience Collaboration
In August 2015, Novartis entered into a global collaboration with Amgen to jointly develop and commercialize pioneering neuroscience treatments in the field of Alzheimer's Disease (AD) and migraine. The companies are partnering in the development and commercialization of a beta-secretase 1 (BACE) inhibitor program in AD. Novartis' oral therapy CNP520 (currently in a Phase II study for AD) will be the lead molecule and further compounds from both companies' pre-clinical BACE inhibitor programs may be considered as novel follow-on molecules. The collaboration also focuses on innovative investigational Amgen drugs in the migraine field, including AMG 334 (currently in Phase III studies for episodic migraine and a Phase II study for chronic migraine) and AMG 301 (currently in a Phase I study for migraine). For the migraine program, Novartis will have global co-development rights and commercial rights outside the U.S., Canada, and Japan.

About 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 currently offer patients and physicians a large drug portfolio encompassing 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 “exciting time,” “committed,” “potential,” “investigating,” “expected,” “being investigated,” “being studied,” “pioneering,” “will,” “may,” “investigational,” “commitment,” “pipeline,” or similar terms, or by express or implied discussions regarding potential marketing approvals for AMG 334, CNP520 and AMG 301, potential new indications or labeling for products in the Novartis Neuroscience portfolio, or regarding potential future revenues from such investigational compounds and products. 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 or AMG 301 will be submitted or approved for sale in any market, or at any particular time. Neither 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. Nor can there be any guarantee that AMG 334, CNP520, AMG 301 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 could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected 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 pressures; unexpected 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, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2015, the Group achieved net sales of USD 49.4 billion, while R&D throughout the Group amounted to approximately USD 8.9 billion (USD 8.7 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit http://www.novartis.com.

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