Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

https://www.novartis.com
https://twitter.com/novartisnews

MEDIA & INVESTOR RELEASE

Novartis announces positive results from a Phase IV study showing superior tolerability and efficacy of Aimovig® (erenumab) compared with topiramate in migraine prevention

- *The first randomized, double blind, head-to-head study of Aimovig® (erenumab) against topiramate in patients with episodic and chronic migraine (HER-MES) achieved superiority in its primary and secondary endpoints*

- *Aimovig showed superior tolerability and efficacy against topiramate and provided a significant reduction in monthly migraine days (MMDs)*

- *Aimovig is the most prescribed anti-calcitonin gene-related peptide pathway (anti-CGRP) therapy worldwide, with more than 480,000 patients prescribed across 44 countries since launch*[1]

Basel, November 02, 2020 — Novartis announced today that HER-MES, the first Phase IV, randomized, double-blind, double-dummy, head-to-head study of Aimovig® (erenumab) against topiramate, an anticonvulsant, in patients with episodic and chronic migraine met its primary and secondary endpoints. The results of HER-MES showed that Aimovig had a superior tolerability and efficacy profile than topiramate, with less discontinuation over the course of the 24-week treatment phase. Aimovig also showed superior efficacy, with a greater proportion of patients achieving at least 50% reduction in their monthly migraine days (MMDs).

“The data generated by this first of a kind head-to-head study reinforces the value of erenumab as a safe and effective migraine prevention treatment. The findings also provide novel insights into migraine therapy for physicians and patients,” said Prof. Uwe Reuter, Managing Medical Director at Charité Universitätsmedizin.

“With Aimovig continuing to be the anti-CGRP treatment with the longest safety and efficacy experience, these results further emphasize its potential to provide significant relief from migraine with an infrequent dosing compared with the oral treatment,” said Estelle Vester-Blokland, Global Head Neuroscience Medical Affairs, Novartis Pharmaceuticals. “Novartis remains fiercely committed to reimagining migraine care worldwide, contributing to the improvement of life for people living with this highly debilitating neurological disease.”

HER-MES aimed to determine the tolerability and efficacy of Aimovig 70 mg and 140 mg compared with topiramate, an anticonvulsant commonly used as standard of care in migraine prevention, in the highest tolerated dose (50-100 mg daily). The study enrolled 777 adult

patients suffering from ≥ 4 MMDs and who were naïve to, not suitable for or had previously failed up to three prophylactic migraine treatments.

The primary outcome of HER-MES explored the Aimovig treatment discontinuation rate due to adverse events compared with topiramate during the double-blind treatment phase of the study. Overall, Aimovig showed superior tolerability against topiramate, with a higher proportion of patients remaining on Aimovig than on topiramate.

The secondary endpoint looked into the superiority of Aimovig compared with topiramate in terms of at least 50% reduction in MMDs to baseline in the last three months of the 24-week, double-blind treatment phase. A higher number of patients in the Aimovig treatment arm experienced a significant (≥50%) reduction in MMDs compared with those on topiramate treatment arm. The safety profile in the HER-MES study was generally consistent with those seen in previous Aimovig clinical trials.

Additional findings and detailed results of primary and secondary endpoints from this trial will be presented at an upcoming scientific congress.

Migraine is a highly debilitating disease that has a significant impact on people's lives, including time spent with family and friends, or at work[2,3]. Aimovig is the first European Medicines Agency (EMA), Swissmedic, and U.S. Food and Drug Administration (FDA)-approved migraine preventive treatment that targets the CGRP receptor (CGRP-R). It is self-administered once monthly via the SureClick® autoinjector, does not require a loading dose and is easy to use[4].

Aimovig is the only CGRP-R inhibitor with up to 5-year clinical trial data in episodic and chronic migraine, adding to the breadth of data showcasing the expanded long-term safety and efficacy of the treatment for migraine patients.

About HER-MES
HER-MES (NCT03828539) is a two-armed, randomized, double-blind, double-dummy, parallel group, Phase IV study to assess the tolerability and efficacy of Aimovig® (erenumab) versus topiramate in a patient-centered setting[5]. The primary endpoint was treatment discontinuation rate due to adverse events compared with topiramate during the double-blind treatment phase of the study[5]. The secondary endpoint was efficacy of 70 mg and 140 mg erenumab versus topiramate in terms of at least 50% reduction in monthly migraine days to baseline in the last three months (months 4, 5 and 6) of the double-blind, 24-week treatment phase[5] in the highest tolerated dose (50-100 mg daily). The HER-MES study enrolled 777 adult patients with episodic or chronic migraine (≥4 migraine days per month) who had not previously received migraine prevention treatment or had unsuccessfully discontinued up to three previous therapies with propranolol/metoprolol, amitriptyline and flunarizine[5]. After a 2-week screening and 4-week baseline phase, patients were randomized 1:1 to erenumab or topiramate. In the double-blind, 24-week treatment phase, patients in the erenumab arm received either 70 mg or 140 mg directly after the baseline phase according to the current expert information, as estimated by the investigator[5]. An increase in dose from 70 mg to 140 mg was possible at any time during the study. Patients in the topiramate arm were given topiramate at the highest tolerated dose (50-100 mg), starting with a 6-week titration phase, according to the latest expert information[5]. The HER-MES study has been fully developed in Germany. The study was conducted in 82 centers from the end of February 2019 to the end of July 2020.

About Aimovig® (erenumab)
Aimovig is the first European Medicines Agency (EMA), Swissmedic, and U.S. Food and Drug Administration (FDA)-approved migraine prevention treatment designed specifically to block the CGRP receptor (CGRP-R), which plays a critical role in migraine. 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 3,000 patients have participated in our overall clinical trial program. This includes 2,600 participants across the

four placebo-controlled pivotal Phase II and Phase III clinical studies as well as participants in further studies such as LIBERTY, a dedicated study in a difficult-to-treat treatment failure population. The most common side effects in the clinical program to date have been viral upper respiratory tract infection, sinusitis, influenza, and back pain. Aimovig is the most prescribed anti-CGRP worldwide, with more than 480,000 patients prescribed in the post-trial setting.

Novartis and Amgen are co-commercializing Aimovig in the US. Amgen has exclusive commercialization rights to the drug in Japan and Novartis has exclusive rights to commercialize in the rest of the world.

About Migraine
Migraine is a distinct neurological disease[6]. 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[7]. Migraine is associated with personal pain, disability, reduced quality of life and financial cost to society[8]. It has a profound and limiting impact on an individual's abilities to carry out everyday tasks; the World Health Organization reported migraine to be one of the top 10 causes of years lived with disability for men and women[8,9]. It remains under-recognized and under-treated[8,10].

Disclaimer
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," "may," "could," "would," "expect," "anticipate," "seek," "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 the investigational or approved products described in this press release, or regarding potential future revenues from such products. 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 the 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. Nor can there be any guarantee that such products 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; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, 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 is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding

innovative ways to expand access to our latest treatments. About 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at **https://twitter.com/novartisnews**
For Novartis multimedia content, please visit **https://www.novartis.com/news/media-library**
For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Novartis Q3 2020 results, October 23, 2020.
2. Lipton R, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology. 2007;68:343–349.
3. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392:1789–1858.
4. Novartis. Data on File. March 2019.
5. ClinicalTrials.gov. Head-to-head Study of Erenumab Against topiRamate-a Double-Blind, Double Dummy Migraine Study to Assess Tolerability and Efficacy a in PatiEnt-Centered Setting. Available from: https://clinicaltrials.gov/ct2/show/NCT03828539 [Last accessed: October 2020].
6. Migraine Research Foundation. Migraine facts. Available from: https://migraineresearchfoundation.org/about-migraine/migraine-facts/ [Last accessed: October 2020].
7. National Institute for Neurological Disorders and Stroke. Migraine Information Page. Available from: https://www.ninds.nih.gov/Disorders/All-Disorders/Migraine-Information-Page [Last accessed: October 2020].
8. World Health Organization. Headache disorders. Available from: http://www.who.int/mediacentre/factsheets/fs277/en/ [Last accessed: October 2020].
9. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388:1545–1602.
10. Diamond S, Bigal ME, Silberstein 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;47:355–363.

# # #

Novartis Media Relations
E-mail: media.relations@novartis.com

Antonio Ligi
Novartis External Communications
+41 79 723 3681 (mobile)
antonio.ligi@novartis.com

Michael Amos
Novartis Global Pharma Communications
+41 79 123 7806 (mobile)
michael.amos@novartis.com

Eric Althoff
Novartis US External Communications
+1 646 438 4335
eric.althoff@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 778 5052
Thomas Hungerbuehler	+41 61 324 8425		
Isabella Zinck	+41 61 324 7188		