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Novartis PARADIGMS data show children and adolescents with MS had an 82% lower relapse rate with Gilenya® vs. interferon beta-1a

- *PARADIGMS data also show patients treated with Gilenya had significantly fewer new brain lesions vs. those on interferon beta-1a*
- *Currently there are no specifically approved disease modifying therapies for children and adolescents with MS, a population at high risk of long-term disability*
- *MS is a highly debilitating disease which touches every aspect of young patients' daily lives, from school performance to family relations and friendships*

Basel, October 28, 2017 – Novartis today announced full results from the positive Phase III PARADIGMS study, investigating the safety and efficacy of Gilenya® (fingolimod) vs. interferon beta-1a, in children and adolescents (ages 10 to 17) with multiple sclerosis (MS). Treatment with oral Gilenya resulted in an 82% reduction in the rate of relapses (annualized relapse rate) over a period of up to two years, compared to interferon beta-1a intramuscular injections ($p < 0.001$)[1]. PARADIGMS is the first ever controlled, randomized trial specifically designed for pediatric MS. The results have been presented at the 7th Joint European and Americas Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS-ACTRIMS) meeting on October 28, 2017 in Paris, France.

"Pediatric MS patients experience more frequent relapses and are more likely to accumulate physical disability at an earlier age than patients diagnosed as adults," said Dr. Tanuja Chitnis, Principle Investigator for PARADIGMS and Director of the Partners Pediatric Multiple Sclerosis Center, Massachusetts General Hospital, Boston, US, and Scientist, Ann Romney Center, Brigham and Women's Hospital, Boston, US. "Yet, current therapies are limited to drugs that have not been tested in a controlled manner in this age group. PARADIGMS was uniquely designed for this patient population. Its results signify an important step towards a potential new treatment that could improve the lives of these young patients."

Additional data from the study demonstrated:

- A significant reduction in the number of new / newly enlarging T2 and Gd-T1 lesions in the brain of Gilenya treated patients compared to those treated with interferon beta-1a, as measured by magnetic resonance imaging (MRI)[1]. The number and volume of lesions are associated with increased relapses and disability progression[2].
- Individuals treated with Gilenya had significantly less brain shrinkage (measured by MRI as brain volume loss), compared to those treated with interferon beta-1a[1]. Brain shrinkage in adults is associated with the loss of physical and cognitive function[3].
- The safety profile of Gilenya was overall consistent with that seen in previous clinical trials, with more adverse events reported in the interferon group[1].
- In an additional analysis, Gilenya significantly delayed disability progression, defined as Confirmed Disability Progression (CDP), compared to interferon beta-1a[1].

"There is already substantial evidence that Gilenya is an effective treatment that improves long-term outcomes for adults with relapsing MS. We are delighted that PARADIGMS has

shown such meaningful benefits for children and adolescents with MS," said Vas Narasimhan, Global Head of Drug Development and Chief Medical Officer, Novartis. "This pioneering study demonstrates our continued commitment to providing new treatment options to MS patients with the highest need. We look forward to working with health authorities and preparing for submission."

Gilenya is not currently approved for the treatment of pediatric MS. Novartis is working on submission with health authorities worldwide.

About the Phase III PARADIGMS study
The Phase III PARADIGMS study (NCT01892722) is a flexible duration (up to two years), double-blind, randomized, multi-center study to evaluate the safety and efficacy of oral Gilenya compared to interferon beta-1a in children and adolescents with a confirmed diagnosis of multiple sclerosis (MS), followed by a five-year open label extension phase[4]. The study enrolled 215 children and adolescents with MS, between the ages of 10 and 17 years with an Expanded Disability Status Scale (EDSS) score between 0 and 5.5[4]. Patients were randomized to receive once-daily oral Gilenya (0.5 mg or 0.25 mg, dependent on patients' body weight) or intramuscular interferon beta-1a once weekly[4].

The primary endpoint of the study was the frequency of relapses in patients treated up to 24 months (annualized relapse rate)[4]. Secondary endpoints include the number of new or newly enlarged T2 lesions, Gadolinium enhancing T1 lesions, safety and the pharmacokinetic properties of Gilenya, all measured throughout the treatment period[4].

The Phase III PARADIGMS study was conducted in 87 sites over 25 countries, and was designed in partnership with the US Food and Drug Administration, the European Medicines Agency and the International Pediatric Multiple Sclerosis Study Group.

About Multiple Sclerosis
Multiple sclerosis (MS) is a chronic disorder of the central nervous system (CNS) that disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss[5]. In adults, there are three types of MS: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS)[6]. In children, RRMS accounts for nearly all cases (approximately 98 percent)[7].

The evolution of MS results in an increasing loss of both physical and cognitive (e.g. memory) function. This has a substantial negative impact on the lives of the approximately 2.3 million people worldwide affected by MS, of which between three and five percent are estimated to be children[8,9].

About Gilenya (fingolimod) in adults
Gilenya (fingolimod) is an oral disease-modifying therapy (DMT) that is highly efficacious at controlling disease activity in relapsing multiple sclerosis (RMS)[10]. Gilenya has a reversible lymphocyte redistribution effect targeting both focal and diffuse central nervous system (CNS) damage caused by MS[11,12]. Long-term clinical trial and real-world evidence and experience has shown Gilenya treatment to be convenient for individuals to incorporate into everyday life, leading to high treatment satisfaction, long-term persistence, and ultimately, improved long-term outcomes for people with RMS[13,14].

Gilenya impacts four key measures of RMS disease activity: relapses, MRI lesions, brain shrinkage (brain volume loss) and disability progression[15,16]. Its effectiveness on all of these measures has been consistently shown in multiple controlled clinical studies and in the real-world setting. Studies have shown its safety and high efficacy to be sustained over the long term, demonstrating that switching to Gilenya treatment as early in the disease course as possible can be beneficial in helping to preserve individuals' function[17,18].

Gilenya is approved in the US for the first-line treatment of relapsing forms of MS in adults, and in the EU for adult patients with highly-active relapsing-remitting MS (RRMS) defined as either high disease activity despite treatment with at least one DMT, or rapidly-evolving severe RRMS[10,19].

Gilenya has been used to treat more than 217,000 patients in both clinical trials and the post-marketing setting, with approximately 480,000 years of patient experience[20].

About Novartis in Multiple Sclerosis
Alongside Gilenya (fingolimod, an S1P modulator), Novartis' multiple sclerosis (MS) portfolio includes Extavia® (interferon beta-1b for subcutaneous injection) which is approved in the US for the treatment of relapsing forms of MS. In Europe, Extavia is approved to treat people with relapsing-remitting MS, secondary progressive MS (SPMS) with active disease and people who have had a single clinical event suggestive of MS.

Investigational compounds include siponimod (BAF312), under investigation in MS, and OMB157 (ofatumumab), a fully human monoclonal antibody under investigation in relapsing MS. OMB157 targets CD20, and is currently being investigated in two Phase III pivotal studies.

In the US, the Sandoz Division of Novartis markets Glatopa® (glatiramer acetate injection) 20mg/mL, the first generic version of Teva's Copaxone®* 20mg.

*Copaxone® is a registered trademark of Teva Pharmaceutical Industries Ltd.

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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," "exciting," "underway," "upcoming," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational and 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; 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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