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Novartis landmark Phase III trial shows fingolimod significantly reduces relapses in children and adolescents with MS

- *Phase III PARADIGMS study in pediatric MS met its primary endpoint, showing a significant reduction in relapses occur with fingolimod versus interferon beta-1a*
- *There is a significant unmet need for safe and effective MS treatments for children and adolescents, for whom there are no specifically approved disease-modifying therapies*
- *Children and adolescents living with MS face physical and cognitive disability that severely limits their ability to go about daily activities, such as going to school*
- *PARADIGMS is a first of its kind study in pediatric MS. Other current treatments have not been evaluated in head to head trials specifically designed for children and adolescents*

Basel, September 05, 2017 – Novartis today announced positive topline results from the Phase III PARADIGMS study, investigating the safety and efficacy of oral once-daily fingolimod in children and adolescents (ages 10 to 17) with multiple sclerosis (MS). Data show that oral fingolimod resulted in a significant and clinically meaningful reduction in the number of relapses (annualized relapse rate) in this patient population over a period of up to two years, compared to interferon beta-1a intramuscular injections[1]. The safety profile of fingolimod was consistent with that seen in other clinical trials, with overall more adverse events reported in the interferon group[1]. The PARADIGMS study is the first ever randomized, controlled Phase III study of a disease-modifying therapy (DMT) in pediatric MS[2].

“Living with MS is a tremendous challenge at any age. However, its appearance in children and adolescents, when these young individuals should be developing and focusing on their future, can be devastating,” said Vas Narasimhan, Global Head of Drug Development and Chief Medical Officer, Novartis. “With no specifically approved treatment options based on a thorough study such as PARADIGMS, the risk of long-term disease progression in these patients is much greater. The outcome of this study is very exciting news for the MS patient community, all of whom benefit from potential advances in high-quality, evidence-based care such as this. I would like to thank the young people with MS and their families, physicians and nurses who participated and made this landmark study possible.”

Results of the Phase III PARADIGMS study will be presented at the 7th Joint ECTRIMS-ACTRIMS meeting, taking place October 25 - 28, 2017, in Paris, France.

Commonly diagnosed during adolescence, pediatric MS is associated with relapses that are more frequent and often more severe than those seen in adults with MS[3]. Relapses negatively affect mobility, balance and cognitive function, and patients with pediatric MS are more likely to accumulate physical disability at an earlier age than those diagnosed as adults[4,5]. There is currently no treatment indicated for children and adolescents living with MS, based on randomized, controlled, clinical study data.

Fingolimod is not currently approved for the treatment of pediatric MS. Novartis plans to complete a thorough analysis of these important data to speak to health authorities to agree on next steps for submission.

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 Phase III study to evaluate the safety and efficacy of oral fingolimod 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[6]. 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[6]. Patients were randomized to receive once-daily oral fingolimod (0.5 mg or 0.25 mg, dependent on patients' body weight) or intramuscular interferon beta-1a once weekly[6].

The primary endpoint of the study was the frequency of relapses in patients treated up to 24 months (annualized relapse rate)[6]. Secondary endpoints include the number of new or newly enlarged T2 lesions, Gadolinium enhancing T1 lesions, safety and the pharmacokinetic properties of fingolimod, all measured throughout the treatment period[6].

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, 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[7]. In adults, there are three types of MS: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS)[8]. In children, RRMS accounts for nearly all cases (approximately 98 percent)[3].

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[5,9].

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 213,000 patients in both clinical trials and the post-marketing setting, with approximately 453,000 years of patient experience[1].

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 BAF312 (siponimod), 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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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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