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Novartis announces EU approval of Gilenya® for children and adolescents with MS, making it the first and only oral disease-modifying treatment for these patients in Europe

- *Approval based on landmark PARADIGMS study showing Gilenya (fingolimod) significantly reduced relapse rates by 82% vs interferon beta-1a; additionally, 85.7% of Gilenya patients were relapse-free at two years*[1]

- *Young people with MS often experience more frequent and severe relapses than adults, which affects their development and ability to participate in daily life*[2]

- *Gilenya, a leading oral MS therapy for adults, now also addresses the critical need for an effective and safe therapy approved for young people living with MS*

Basel, November 29, 2018 – Novartis today announced that the European Commission (EC) has approved Gilenya® (fingolimod) for the treatment of children and adolescents 10 to 17 years old with relapsing-remitting forms of multiple sclerosis (RRMS). The European market authorization makes Gilenya the first and only oral disease-modifying treatment for children and adolescents based on clinical Phase III data. This young population living with MS have a critical need for an effective treatment option, as they experience two-to-three times as many relapses as adults, often leading to a more severe prognosis and earlier irreversible disability compared to adult-onset MS[2].

“We are excited by the news that there is now a new approved treatment indicated for young people with RRMS in Europe – hopefully this will be the first step to having more therapy options for children and adolescents with MS,” said Pedro Carrascal, President, European Multiple Sclerosis Platform. “Young patients affected by MS often experience a more severe impact during their overall lifetime. Today’s approval provides an opportunity for a brighter future for them and their families.”

“Early onset MS can have a devastating impact on children and adolescents’ daily life, such as going to school and spending time with friends and family,” said Paul Hudson, Chief Executive Officer, Novartis Pharmaceuticals. “Our mission is to change the course of MS as we’ve been doing since the treatment’s initial approval in 2011, and we won’t stop until we stop MS. We are delighted that today’s decision has brought us one step closer to reimagining the treatment of MS, across all ages.”

The EC’s approval is based on the PARADIGMS trial, a landmark Phase III clinical study in MS, specifically designed for children and adolescents 10 to 17 years old[1]. Results from the double-blind, randomized, multi-center study of Gilenya vs. interferon beta-1a show that Gilenya significantly reduced the annualized relapse rates by 82% (compared to interferon beta-1a, $p<0.001$) and 85.7% of patients treated with Gilenya were relapse-free at up to 24 months, versus 38.8% of patients treated with interferon beta-1a ($p<0.001$)[1]. Patients treated with Gilenya also showed a 77% risk reduction of disability progression relative to patients treated with interferon beta-1a[1]. Furthermore, it also significantly reduced the number of new or newly enlarged T2 lesions up to 24 months by 53% (compared to interferon beta-1a, $p<0.001$) and the annualized rate of brain volume loss (brain shrinkage) by 40% (compared to

interferon beta-1a, p=0.014)[1]. The full PARADIGMS data were published in *The New England Journal of Medicine* in September 2018.

The EC decision is applicable to all 28 European Union member states plus Iceland, Norway and Liechtenstein. Gilenya was initially approved for adults aged 18 years and older with relapsing forms of multiple sclerosis in the US and Europe. Gilenya received FDA approval for the treatment of children and adolescents 10 years of age and older with MS on May 11, 2018.

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 injectable interferon beta-1a in children and adolescents with a confirmed diagnosis of multiple sclerosis (MS), followed by a five-year open label extension phase[1]. The study enrolled 215 children and adolescents with MS, from 10 to less than 18 years of age with an Expanded Disability Status Scale (EDSS) score between 0 and 5.5[1]. 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[1].

The primary endpoint of the study was the frequency of relapses in patients treated up to 24 months (annualized relapse rate)[1]. 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[1].

The PARADIGMS study enrolled 215 patients at 80 centers in 25 countries and was designed in agreement 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[3]. In adults, there are three main types of MS: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS)[4]. Approximately 85% of people with MS have relapsing-remitting MS, where the immune system attacks healthy tissue[5]. In children, RRMS account for nearly all cases (approximately 98%)[6].

About Novartis in Multiple Sclerosis
The Novartis multiple sclerosis portfolio includes Gilenya® (fingolimod, an S1P modulator), which is indicated for relapsing forms of MS. In the United States, Gilenya is the first disease-modifying therapy approved for the treatment of children and adolescents 10 to less than 18 years of age with relapsing forms of multiple sclerosis (RMS).

Investigational compounds include siponimod (BAF312). Siponimod is an investigational, selective modulator of specific subtypes of the sphingosine-1-phosphate (S1P) receptor, and has the potential to delay progression and expand possibilities for patients with typical SPMS. Novartis initiated the submission of siponimod for US approval in SPMS in the first half of 2018, which was followed by filing with the EMA in September 2018 for EU approval. The file has been accepted by both agencies.

Our other investigational compound is subcutaneously administered ofatumumab (OMB157), a fully human monoclonal antibody in development for relapsing MS. Ofatumumab targets CD20, and is currently being investigated in two Phase III pivotal studies.

Extavia® (interferon beta-1b for subcutaneous injection) 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.

In the US, the Sandoz Division of Novartis markets Glatopa® (glatiramer acetate injection) 20 mg/mL and 40 mg/mL, generic versions of Teva's Copaxone®.

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

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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 1 billion people globally and we are finding innovative ways to expand access to our latest treatments. About 125 000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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