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## **Novartis announces FDA approval of Gilenya® as the first disease-modifying therapy for pediatric relapsing multiple sclerosis**

- *New approval for Gilenya (fingolimod) addresses strong unmet need for younger patients, who often experience more frequent relapses than adults with multiple sclerosis (MS)<sup>1</sup>*
- *In a landmark controlled Phase III study of children and adolescents (ages 10 to less than 18) with relapsing forms of MS (RMS), Gilenya reduced the annualized relapse rate by approximately 82% vs. interferon beta-1a injections ( $p < 0.001$ )<sup>2</sup>*
- *Gilenya is the most prescribed oral once-daily MS disease-modifying treatment, with a global exposure of more than 231,000 patients since its initial approval for adults with RMS<sup>3</sup>*

**Basel, May 11, 2018** – Novartis today announced that the US Food and Drug Administration (FDA) has approved Gilenya® (fingolimod) for the treatment of children and adolescents 10 to less than 18 years of age with relapsing forms of multiple sclerosis (RMS), making it the first disease-modifying therapy indicated for these patients<sup>2</sup>.

This approval expands the age range for Gilenya, which was previously approved for patients aged 18 years and older with RMS. Gilenya was granted Breakthrough Therapy designation by the FDA in December of 2017 for this pediatric indication.

“We now finally have an FDA-approved treatment for children and adolescents with relapsing MS,” said Dr. Brenda Banwell, Chief of the Division of Neurology at Children’s Hospital of Philadelphia, who served as co-Principal investigator of the pivotal study that supported the pediatric approval. “Repeated relapses are more common in young people with MS than in adults, so this is heartening news for patients and their families.”

While MS is mostly diagnosed in adults, children and adolescents with the chronic disease often experience more frequent relapses and brain lesions than adults with MS<sup>1</sup>.

“Since revolutionizing the treatment of relapsing MS as the first oral disease-modifying therapy, Gilenya has become an important mainstay of treatment for adult patients,” said Paul Hudson, CEO, Novartis Pharmaceuticals. “Today’s announcement is a result of our pioneering approach and ongoing commitment to advancing care for all individuals living with MS, and we are delighted this has led to a long-awaited, specifically-approved treatment option for young patients.”

The approval of Gilenya for the younger patient population was supported by PARADIGMS, a double-blind, randomized, multi-center Phase III safety and efficacy study of Gilenya vs. interferon beta-1a, designed specifically for children and adolescents with RMS<sup>4</sup>. The primary endpoint demonstrated that Gilenya reduced the rate of relapses (annualized relapse rate) by approximately 82% ( $p < 0.001$ ) over a period of up to two years compared to interferon beta-

1a intramuscular injections in children and adolescents (ages 10 and older) with relapsing MS<sup>2</sup>. The safety profile of Gilenya in this study was overall consistent with that seen in previous clinical trials in adults<sup>2</sup>.

#### **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<sup>5</sup>. The study enrolled 215 children and adolescents with MS, 10 to less than 18 years of age with an Expanded Disability Status Scale (EDSS) score between 0 and 5.5<sup>5</sup>. 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<sup>5</sup>.

The primary endpoint of the study was the frequency of relapses in patients treated up to 24 months (annualized relapse rate)<sup>5</sup>. 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<sup>5</sup>.

The PARADIGMS study was conducted in 87 sites over 26 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<sup>6</sup>. In adults, there are three types of MS: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS)<sup>7</sup>. Approximately 85 percent of people with MS have relapsing-remitting MS, where the immune system attacks healthy tissue.<sup>8</sup> In children, RRMS accounts for nearly all cases (approximately 98 percent)<sup>9</sup>.

In the US, MS affects around 400,000 people<sup>10</sup>.

#### **About Gilenya (fingolimod) in Adults**

Gilenya<sup>®</sup> (fingolimod) is an oral disease-modifying therapy (DMT) that is highly efficacious at controlling disease activity in relapsing multiple sclerosis (RMS). Gilenya has a reversible lymphocyte redistribution effect targeting both focal and diffuse central nervous system (CNS) damage caused by MS. 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.

Gilenya impacts four key measures of RMS disease activity: relapses, MRI lesions, brain shrinkage (brain volume loss) and disability progression. 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.

Gilenya is approved in the US for the first-line treatment of relapsing forms of MS, 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.

Gilenya has been used to treat more than 231,000 patients in both clinical trials and the post-marketing setting, with approximately 536,000 years of patient experience<sup>3</sup>.

#### **About Novartis in Multiple Sclerosis**

Alongside Gilenya (fingolimod, an S1P modulator), Novartis' multiple sclerosis (MS) portfolio includes Extavia<sup>®</sup> (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<sup>®</sup> (glatiramer acetate injection) 20 mg/mL and 40 mg/mL, generic versions of Teva's Copaxone<sup>®\*</sup>.

\*Copaxone<sup>®</sup> is a registered trademark of Teva Pharmaceutical Industries Ltd.

#### **Disclaimer**

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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 2017, the Group achieved net sales of USD 49.1 billion, while R&D throughout the Group

amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 124,000 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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