Novartis receives positive CHMP opinion for Gilenya® for the treatment of children and adolescents with MS, marking a major medical advance for young MS patients in Europe

- Children and adolescents with multiple sclerosis (MS) experience more frequent and often more severe relapses than adults with the disease, hindering their development and ability to take part in everyday life.

- Positive opinion is based on the landmark Phase III PARADIGMS trial, which showed Gilenya (fingolimod) substantially reduced the debilitating impact of MS in young patients.

- If approved, Gilenya is expected to be the first and only oral disease-modifying therapy approved for children and adolescents in Europe.

Basel, September 21, 2018 – Novartis today announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has recommended approval of Gilenya® (fingolimod) for the treatment of children and adolescents 10 to 17 years of age with relapsing remitting forms of multiple sclerosis (RRMS). If approved, Gilenya® is expected to be the first oral disease-modifying therapy indicated for these patients based on a randomized controlled clinical study1. The younger patient population experiences two-to-three times as many relapses as adults, often leading to a more severe prognosis and earlier disability compared to adult-onset MS2. If approved, Gilenya would address the urgent need faced by these young people. This market authorization would expand the age range of Gilenya, one of the most prescribed MS treatments worldwide. Gilenya was previously approved for adults with RRMS aged 18 years and older in Europe.

"The lives of kids are immensely impacted by the early onset of MS, from playing sports, going to school or enjoying time with friends and family. We need to address the urgent need for new and effective treatments, and with Gilenya, we may now have an option that can make a substantial difference for young patients", said Paul Hudson, Chief Executive Officer, Novartis Pharmaceuticals. "This CHMP positive opinion is a testament to our relentless dedication to reimagining MS care across all generations. We are very excited to be a step closer to bringing this much-needed treatment to young MS patients across Europe."

"Today's CHMP positive opinion is a momentous advancement for the children and adolescents impacted by MS," said Pedro Carrascal, President, European Multiple Sclerosis Platform. "Young European patients and their families, who have long been hoping for an effective disease modifying therapy, could soon have a new treatment option to alleviate the devastating impact of this condition."

The CHMP positive opinion is based on the PARADIGMS trial, a first-of-its-kind clinical study in MS specifically designed for children and adolescents aged 10 to 17 years3. Results from
the double-blind, randomized, multi-center Phase III study of Gilenya vs. interferon beta-1a show that compared to interferon beta-1a, Gilenya significantly reduced the annualized relapse rates by 82% (relative difference to interferon beta-1a, p<0.001) and delayed the time to first relapse\(^4\). Furthermore, it also significantly reduced the number of new or newly enlarged T2 lesions up to 24 months by 53% (p<0.001) and the annualized rate of brain volume loss (brain shrinkage) by 40%\(^4\). The full PARADIGMS data was recently published in *The New England Journal of Medicine*.

The European Commission will review the CHMP opinion and is expected to deliver its final decision within three months. The decision will be applicable to all 28 European Union member states plus Iceland, Norway and Liechtenstein. 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\(^4\). 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 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\(^5\). In adults, there are three main types of MS: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS)\(^6\). Approximately 85% of people with MS have relapsing-remitting MS, where the immune system attacks healthy tissue\(^7\). In children, RRMS account for nearly all cases (approximately 98%)\(^8\).

**About Novartis in Multiple Sclerosis**
Alongside Gilenya (fingolimod, an S1P modulator), the Novartis multiple sclerosis (MS) portfolio includes Extavia\(^\circledast\) (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 SPMS, 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\(^\circledast\) (glatiramer acetate injection) 20 mg/mL and 40 mg/mL, generic versions of Teva’s Copaxone\(^\circledast\)*.

*Copaxone\(^\circledast\) 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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