Novartis announces FDA and EMA filing acceptance of siponimod, the first and only drug shown to meaningfully delay disability progression in typical SPMS patients

- There is a critical need for safe and effective treatments for secondary progressive multiple sclerosis (SPMS) – a highly debilitating form of MS characterized by gradual, irreversible worsening of disability, largely independent of relapses
- If approved, siponimod (BAF312) would be the first oral disease-modifying therapy with the potential to delay progression and expand possibilities for SPMS patients
- Filings are supported by Phase III EXPAND data, which showed siponimod had beneficial effects on disability, relapses and magnetic resonance imaging (MRI) disease activities in typical SPMS patients
- Novartis used a priority review voucher to expedite review of siponimod in the US to ensure patients could benefit from the drug as soon as possible, pending approval

Basel, October 08, 2018 – Novartis today announced that both the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) have accepted the company’s New Drug Application (NDA) and Marketing Authorization Application (MAA) respectively, for investigational oral, once-daily siponimod (BAF312) for the treatment of secondary progressive multiple sclerosis (SPMS) in adults. This phase of multiple sclerosis (MS) can substantially impact lives, due to physical and cognitive impairments. To bring this treatment to the MS community as quickly as possible, Novartis used a review voucher to expedite the review of siponimod in the US. Regulatory action for siponimod is anticipated in the US in March of 2019 and in Europe in late 2019.

More than 80% of people with relapsing-remitting MS (RRMS) – the most common form of the condition at diagnosis – go on to develop SPMS, with or without relapses. SPMS is a form of MS that leads to progressive, irreversible disability, such as the need for enhanced walking aids and wheelchairs, bladder dysfunction and cognitive decline, largely independent of relapses. Following the initial RRMS course, there is a gradual increase in the number of patients transitioning to SPMS, with around 25% progressing by 10 years post-onset, 50% by 20 years and more than 75% by 30 years.

“We are excited to see a potential new treatment on the horizon,” said Bruce Bebo, Executive Vice President Research, National MS Society, United States. “It is a significant milestone in our unrelenting search for treatments that can benefit adults living with secondary progressive MS who currently have few options.”

“Siponimod is the first investigational medicine to show a significant delay in disability progression in typical SPMS patients,” said Paul Hudson, Chief Executive Officer, Novartis
Pharmaceuticals. “With siponimod, we underpin our strong commitment to the MS community by reimagining care for people whose lives have been considerably disrupted by this devastating illness. We are closely working with the FDA and EMA to ensure siponimod is available for patients as soon as possible.”

The regulatory application is based on data from the EXPAND study, a randomized, double-blind, placebo-controlled Phase III study, comparing the efficacy and safety of siponimod versus placebo in people living with typical SPMS. At study initiation, more than 50% of patients in the EXPAND study relied on a walking aid. Results from the pivotal study showed siponimod significantly reduced the risk of three-month confirmed disability progression versus placebo (primary endpoint; 21% versus placebo, p=0.013). Siponimod also meaningfully delayed the risk of six-month confirmed disability progression (26% vs placebo, p=0.0058) and demonstrated favorable outcomes in other relevant measures of MS disease activity and progression. Further, more advanced analyses of the EXPAND study showed that siponimod reduced the risk of disability progression largely disassociated from relapses (three-month disability progression, range 14-20%; six-month disability progression 29-33%).

In addition, Novartis conducted the BOLD study, a randomized, double-blind, placebo-controlled, adaptive dose-ranging, Phase II study in patients with RRMS. The study showed that siponimod significantly reduced the annualized rate of relapses (ARR) over six months compared to placebo (ARR siponimod 2 mg vs. placebo 0.20 vs. 0.58 (p=0.041)).

In Switzerland, Swissmedic granted fast track authorization procedure for siponimod in SPMS. Discussions with additional health authorities regarding siponimod are ongoing.

**About Siponimod (BAF312)**
Siponimod is an investigational, selective modulator of specific subtypes of the sphingosine-1-phosphate (S1P) receptor. Siponimod binds to the S1P1 sub-receptor on lymphocytes, which prevents them from entering the central nervous system (CNS) of patients with multiple sclerosis. This leads to the anti-inflammatory effects of siponimod. Siponimod also enters the CNS and binds to the S1P5 sub-receptor on specific cells in the CNS (oligodendrocytes and astrocytes). By binding to these specific receptors, siponimod has the potential to modulate damaging cell activity, and preclinical studies suggest that it may prevent synaptic neurodegeneration and promote remyelination in the CNS.

**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. In adults, there are three types of MS: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS). Approximately 85% of people with MS have RRMS, where the immune system attacks healthy tissue. In children and adolescents, RRMS accounts for nearly all cases (approximately 98%).

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 or adolescents.

**About Novartis in Multiple Sclerosis**
Alongside Gilenya® (fingolimod, a modulator of the S1P receptor subtypes 1,3,4 and 5), the 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, a selective modulator of the S1P receptor subtypes 1 and 5), for SPMS, and 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.

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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