Novartis announces FDA filing acceptance of siponimod (BAF312), the first and only oral drug shown to delay disability progression in typical SPMS patients

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- - 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 for SPMS patients
- - Filing is supported by the Phase III EXPAND data, which showed siponimod had beneficial effects on disability, relapses and MRI disease activities in typical SPMS patients[1]
- - 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

EAST HANOVER, N.J., Oct. 8, 2018 /PRNewswire/ -- Novartis today announced that the US Food and Drug Administration (FDA) has accepted the company's New Drug Application (NDA) 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 vision impairment, fatigue, dependence on walking aids and inability to work[2]. To bring this treatment to the MS community as quickly as possible, Novartis used a priority review voucher to expedite the review of siponimod. Regulatory action for siponimod is anticipated in March of 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[2,3]. 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[2,3].

"As people with MS have lived with the disease for decades, new treatment options can make a significant impact on the course of their illness, especially as their MS changes over time," said Fabrice Chouraqui, Novartis Pharmaceuticals Corporation. "If approved, siponimod would be the first oral treatment approved for SPMS that significantly delays disability progression. We look forward to working with the FDA to make it available to people living with MS as quickly 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[1]. 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[1].

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 reduced not only the number of combined unique active lesions (primary outcome) but also reduced the rate of annual relapses (secondary endpoint) over six months compared to placebo.[4]

"We are excited to see a potential new treatment on the horizon," said Bruce Bebo, Executive Vice President, Research, National MS Society. "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."

Additionally, the European Medicines Agency (EMA) has accepted the company's Marketing Authorization Application (MAA) for siponimod. Regulatory action for siponimod in Europe is anticipated in late 2019.

About Siponimod (BAF312)
Siponimod is an investigational, selective modulator of specific subtypes of the sphingosine-1-phosphate (S1P) receptor[5]. 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.[1] Siponimod also enters the CNS and binds to the S1P5 sub-receptor on specific cells in the CNS (oligodendrocytes and astrocytes) [6]. 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 central nervous system[7].

About Multiple Sclerosis
MS is a chronic disorder of the CNS that affects around 400,000 people in the US[8]. There are three main types of MS: RRMS, SPMS and primary progressive MS (PPMS)[9]. MS disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss[10]. The evolution of the MS results in an increasing loss of both physical (e.g., walking) and cognitive (e.g., memory) function.

SPMS follows an initial phase of RRMS, which accounts for approximately 85% of all MS diagnoses, and is characterized by gradual worsening of neurological function over time[11]. This leads to a progressive accumulation of disability, largely independent of relapses, which can severely affect patients' abilities to carry out everyday activities[11]. There remains a high unmet need for effective and safe treatments to help delay disability progression in SPMS[12].

Novartis in Neuroscience
Novartis has a strong ongoing commitment to neuroscience and to bringing innovative treatments to patients suffering from neurological conditions where there is a high unmet need. We are committed to supporting patients and physicians in multiple disease areas, including Multiple Sclerosis (MS), Alzheimer's disease, Parkinson's disease, Epilepsy and Attention Deficit Hyperactivity Disorder, and have a promising pipeline in MS, Alzheimer's disease, migraine and specialty neurology (e.g., neuropathic pain).

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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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