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MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG

Novartis announces EU approval of Mayzent® (siponimod) for adult patients with secondary progressive multiple sclerosis (SPMS) with active disease

- *Mayzent® (siponimod) is the first and only oral treatment specifically indicated for patients with secondary progressive multiple sclerosis (SPMS) with active disease in Europe[1]*
- *Mayzent addresses an unmet need for SPMS patients with active disease who, until now, did not have an oral treatment that has been shown to be effective in delaying progression in this patient population*
- *Approval is based on the Phase III EXPAND trial, the largest randomized clinical study in a broad range of SPMS patients, showing Mayzent significantly reduced the risk of disease progression, including physical disability and cognitive decline[2,3]*

Basel, January 20, 2020 — Novartis today announced the European Commission (EC) has approved Mayzent® (siponimod) for the treatment of adult patients with secondary progressive multiple sclerosis (SPMS) with active disease evidenced by relapses or imaging features of inflammatory activity. Although every patient's MS journey is unique, up to 80% of relapsing remitting MS (RRMS) patients will eventually transition to SPMS[4]. Mayzent addresses an unmet need for SPMS patients with active disease who, until now, did not have an oral treatment that has been shown to be effective in delaying progression in this patient population. The European marketing authorization makes Mayzent the first and only indicated oral treatment proven in SPMS patients with active disease based on a randomized clinical trial of a broad range of SPMS patients.

"We are delighted by the news that there is now a treatment available for people in Europe living with active SPMS to potentially delay the progression of this debilitating disease," said Pedro Carrascal, President of the European MS Platform. "This treatment brings hope for improved care and quality of life to patients who have long been underserved."

The EC's approval is based on data from the EXPAND study, a randomized, double-blind, placebo-controlled trial, comparing the efficacy and safety of Mayzent versus placebo in a broad range of SPMS patients (EDSS score 3·0–6·5 at baseline). EXPAND included a subgroup of patients with active disease (n=779), defined as patients with relapses in the two years prior to the study and/or presence of Gd-enhancing T1 lesions at baseline. The baseline characteristics were similar except for signs of activity compared to the overall population.

In the subgroup of Mayzent-treated patients with active disease, results showed:

- The risk of three-month and six-month confirmed disability progression (CDP) was significantly reduced by 31% compared to placebo and by 37% compared to placebo, respectively[5].
- Significant favorable outcomes in other relevant measures of MS disease activity, including annualized relapse rate (ARR – confirmed relapses), MRI disease activity and brain volume loss (brain shrinkage)[5].

Results in the overall population showed that Mayzent significantly reduced the risk of three-month CDP (primary endpoint; 21% reduction versus placebo, p=0.013) and meaningfully delayed the risk of six-month CDP (26% versus placebo, p=0.0058)[2]. Mayzent also has a meaningful benefit on cognition and demonstrated clinically relevant effects on cognitive processing speed[5].

“As the only indicated oral therapy proven for people living with SPMS with active disease, we are pleased that the European approval of Mayzent will help change the conversation about progressing MS and expand possibilities for patients and their caregivers,” said Max Bricchi, Global Head, Neuroscience Franchise, Novartis Pharmaceuticals. “Delaying progression is hugely important for people living with MS who want to maintain independence longer and today’s decision gives them a chance to achieve this goal. We are dedicated in our mission to reimagine medicine and enable brighter futures for people with severe progressive diseases like MS.”

Novartis is working closely with all stakeholders to ensure that eligible European patients can start benefitting from this treatment as quickly as possible. In March 2019, Novartis received approval from the US Food and Drug Administration (FDA) for Mayzent for the treatment of relapsing forms of multiple sclerosis (RMS), to include clinically isolated syndrome (CIS*), relapsing remitting disease, and active secondary progressive disease, in adults. In November 2019, Novartis received approval from the Australian Therapeutic Goods Administration (TGA) for Mayzent for adult patients with SPMS. Novartis is committed to bringing Mayzent to patients worldwide, and additional regulatory filings are currently underway in Switzerland, Japan, Canada and China.

About Mayzent® (siponimod)
Mayzent is a sphingosine 1-phosphate receptor modulator that selectively binds to S1P1 and S1P5 receptors. In relation to the S1P1 receptor, it prevents the lymphocytes from egressing the lymph nodes and as a consequence, from entering the central nervous system (CNS) of patients with MS[2]. This leads to the anti-inflammatory effects of Mayzent[6]. Mayzent also enters the CNS[7,8,9] and binds to the S1P5 sub-receptor on specific cells in the CNS, including astrocytes and oligodendrocytes and has shown pro-remyelinating and neuroprotective effects in preclinical models of MS[10,11,12].

In the European Union (EU), Mayzent is indicated for the treatment of adult patients with SPMS with active disease evidenced by relapsing or imaging features of inflammatory activity. In the US, Mayzent is approved for the treatment of relapsing forms of MS, to include CIS*, relapsing remitting disease and active secondary progressive disease. In November 2019, Novartis received approval from the Australian TGA for Mayzent for adult patients with SPMS. The approvals in the US, Australia, and EU are based on the Phase III EXPAND trial, the largest controlled clinical study of a broad range of SPMS patients, showing Mayzent significantly reduced the risk of disease progression, including impact on physical disability and cognitive decline[2]. Novartis is committed to bringing Mayzent to patients worldwide, and additional regulatory filings are currently underway in Switzerland, Japan, Canada and China.

About the EXPAND Study[2]
EXPAND is a randomized, double-blind, placebo-controlled Phase III study, comparing the efficacy and safety of Mayzent versus placebo in people with SPMS with varying levels of disability, EDSS scores of 3·0–6·5. It is the largest randomized, controlled study in SPMS to date, including 1,651 people with a diagnosis of SPMS from 31 countries. Mayzent

demonstrated a safety profile that was overall consistent with the known effects of S1P receptor modulation. It reduced the risk of three-month CDP by a statistically significant 21% (p=0.013; primary endpoint). CDP was defined as a 1-point increase in EDSS, if the baseline score was 3·0–5·0, or a 0·5-point increase, if the baseline score was 5·5–6·5. No significant differences were found in the Timed 25-Foot Walk Test. T2 lesion volume was reduced by 79% as compared to placebo. Additional secondary endpoints included a relative reduction in the ARR by 55%, and compared to placebo, more patients were free from Gd-enhancing lesions (89% vs 67% for placebo) and from new or enlarging T2 lesions (57% vs 37% for placebo). Additional exploratory analyses presented at the 35th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), demonstrated Mayzent can help patients keep their mobility for over four years longer on average[13†].

About Multiple Sclerosis
MS disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss[14]. MS, which affects approximately 2.3 million people worldwide[4], is often characterized into three forms: primary progressive MS (PPMS)[15], relapsing-remitting MS (RRMS), and SPMS, which follows from an initial RRMS course and is characterized by physical and cognitive changes over time, in presence or absence of relapses, leading to a progressive accumulation of neurological disability[16]. Approximately 85% of patients initially present with relapsing forms of MS[4]. There remains a high unmet need for safe and effective treatments to help delay disability progression in SPMS with active disease (with relapses and/or evidence of new MRI activity)[16].

About Novartis in MS
In addition to Mayzent, the Novartis MS portfolio includes also Gilenya® (fingolimod, an S1P modulator), which is indicated in the EU for the treatment of adult patients and children and adolescents 10 years of age and older with RRMS. In the United States, Gilenya is approved for the treatment of adults and pediatric patients aged 10 years and older with RMS, to include CIS*, relapsing remitting disease and active secondary progressive disease.

Ofatumumab (OMB157), a fully human anti-CD20 monoclonal antibody (mAb) that targets B-cells, is in development for treating RMS. Positive Phase III data presented in September 2019 show ofatumumab met primary endpoints to reduce the ARR in patients with RMS[17]. If approved, ofatumumab will potentially become a treatment for a broad RMS population and the first subcutaneous B-cell therapy that can be self-administered at home.

Extavia® (interferon beta-1b for subcutaneous injection) is approved in the US for RMS, to include CIS*, relapsing remitting disease and active secondary progressive disease. In Europe, Extavia is approved to treat people with RRMS, 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) 20mg/mL and 40mg/mL, generic versions of Teva's glatiramer acetate.

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approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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 more than 750 million people globally and we are finding innovative ways to expand access to our latest treatments. About 109,000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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*Clinically isolated syndrome (CIS) is defined as a first episode of neurologic symptoms that lasts at least 24 hours and is caused by inflammation or demyelination in the central nervous system[18].
†As measured by prolonged time to wheelchair dependence for patients with SPMS by an average of 4.3 years versus placebo.

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