New Novartis analyses at AAN show siponimod’s efficacy on disability and cognition in secondary progressive MS patients

- Analyses of the EXPAND study showed that siponimod (BAF312) reduced the risk of disability progression largely disassociated from relapses in patients with secondary progressive multiple sclerosis (SPMS)

- In EXPAND, siponimod also had a meaningful benefit on patients’ cognitive processing speed

- Findings add to clinical evidence for siponimod in SPMS, an area with a high unmet need for well-tolerated and effective new therapies

Basel, April 20, 2018 – Novartis today announced new analyses from the Phase III EXPAND study of oral, once-daily siponimod (BAF312) in patients with secondary progressive multiple sclerosis (SPMS). In pre-specified statistical analyses, treatment with siponimod consistently reduced the risk of confirmed disability progression in SPMS patients, with and without relapses. In addition, new post-hoc analyses using more accurate methods to estimate the treatment effect on disability progression, now substantiate that the risk reduction with siponimod is largely disassociated from relapses. Siponimod also showed a significant benefit on cognitive processing speed, the key cognitive function impacted by MS, which frequently deteriorates in people with the disease. These results are being presented at the 70th American Academy of Neurology (AAN) Annual Meeting, in Los Angeles, USA, April 21-27, 2018.

As previously reported for the overall study population, treatment with siponimod resulted in a statistically significant risk reduction in disability progression sustained for three- and six-months. The new EXPAND study analyses, using a more advanced model-based approach, show an estimated risk reduction for disability progression, sustained at three-months that ranged from 14-20% compared to placebo (calculated by principal stratum analysis) for non-relapsing patients. For disability sustained at six-months, estimated risk reduction was even greater, spanning from 29-33%. Other complementary statistical approaches assessing the effect of siponimod on disability progression disassociated from relapses showed consistent results.

“Siponimod’s beneficial effect on preventing disability progression, independent from its reduction in relapse frequency, demonstrates that patients with secondary progressive MS could benefit from this treatment,” said study steering committee member Bruce Cree, MD, PhD, MAS, Clinical Research Director and Associate Professor, University of California, San Francisco, School of Medicine. “This is very exciting because many people diagnosed with relapsing-remitting MS, the most common form of the disease, will ultimately transition to SPMS, where without effective new therapies, they experience gradual worsening of disability despite infrequent relapses.”

In pre-specified and post hoc analyses, siponimod’s effect on cognitive processing speed was evaluated, as measured by the Symbol Digit Modalities Test (SDMT). SDMT is the only
cognitive test with established clinical relevance of change in MS and is widely accepted by patients and physicians. Other tests included the Paced Auditory Serial Addition Test (PASAT, assessing cognitive processing speed) and the Brief Visuospatial Memory Test-Revised (BVMT-R, assessing memory). From baseline to month 24, treatment with siponimod showed a significant benefit on cognitive processing speed, compared to placebo, for all patients (SDMT, p=0.0004), and also in those who had relapses within two years before starting the trial (SDMT p=0.0151; PASAT p=0.0275) and those who did not (SDMT p=0.0099; PASAT not statistically significant). Treatment with siponimod did not result in significant differences in memory (BVMT-R).

“A decline in the ability to rapidly process information affects more than half of MS patients and is more severe in secondary progressive MS than relapsing-remitting MS. These data show that siponimod could have a meaningful impact on these patients’ daily lives,” said Danny Bar-Zohar, Global Head Neuroscience Development, Novartis. “Furthermore, the advanced models used in the new analyses help us to better understand the relationship between relapses and disability and the effect of siponimod on these parameters. We are encouraged by these latest findings, which further solidify the clinical evidence for siponimod as a potential new, much needed treatment option for SPMS.”

Novartis has initiated the submission of siponimod for US approval in SPMS in the first half of 2018. Filing for EU approval is planned to follow later in 2018.

About the EXPAND study
The EXPAND study is a randomized, double-blind, placebo-controlled Phase III study, comparing the efficacy and safety of siponimod versus placebo in people with secondary progressive MS (SPMS). It is the largest randomized, controlled study in SPMS to date, and included 1,651 people with SPMS from 31 countries. At the time of the study, individuals enrolled in EXPAND had a mean age of 48 years and had been living with MS for approximately 17 years. Patients had received a diagnosis of SPMS, and also demonstrated progression of disability in the two years prior to study. They also had an Expanded Disability Status Scale (EDSS) score between 3.0 and 6.5 inclusive, with a median score of 6.0, which corresponds to the use of a unilateral walking aid (e.g., a cane or a crutch). Patients were randomized to receive either 2mg siponimod once-daily or placebo, in a 2:1 ratio. Patients continued on siponimod treatment in the open-label long-term extension part of the study.

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 and is believed to contribute 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 may help to reduce the loss of neurological function associated with SPMS. The receptor specificity and pharmacokinetic properties of siponimod facilitate treatment initiation, and contribute to its safety and convenience profile.

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. The evolution of MS results in an increasing loss of both physical (e.g. walking) and cognitive (e.g. memory) function. There are three main types of MS: relapsing remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS).
SPMS is characterized by gradual worsening of neurological function over time. This leads to a progressive accumulation of disability, largely disassociated from relapses, which can severely affect patients’ abilities to carry out everyday activities. It follows an initial phase of RRMS, which accounts for approximately 85% of all MS diagnoses; almost a quarter of people with RRMS will go on to develop SPMS within 10 years of their initial RRMS diagnosis, rising to more than three-quarters after 30 years. There remains a high unmet need for effective and safe treatments to help delay disability progression and improve cognition in SPMS.

MS affects approximately 2.3 million people worldwide.

About Novartis in Multiple Sclerosis
The Novartis multiple sclerosis (MS) portfolio includes Gilenya® (fingolimod, an S1P modulator), which is indicated for relapsing forms of MS and is also in development for pediatric MS. Extavia® (interferon beta-1b for subcutaneous injection) 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 sipoimod (BAF312), under investigation in MS, 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.

Disclaimer
This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “plan,” “expect,” “anticipate,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or 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; 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 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.

Novartis is on Twitter. Sign up to follow @Novartis at http://twitter.com/novartis
For Novartis multimedia content, please visit http://www.novartis.com/news/media-library
For questions about the site or required registration, please contact media.relations@novartis.com

References
6. Drake AS et al. Psychometrics and normative data for the Multiple Sclerosis Functional Composite: replacing the PASAT with the Symbol Digit Modalities Test. Mult Scler. 2010; 16(2); 228-237.
14. Aslanis V et al. Siponimod (BAF312) (and/or its metabolites) penetrates into the CNS and distributes to white matter areas. Mult Scler J. 2012; 18(10); suppl. P792.
Novartis Media Relations
Central media line: +41 61 324 2200
E-mail: media.relations@novartis.com

Eric Althoff
Novartis Global Media Relations
+41 61 324 7999 (direct)
+41 79 593 4202 (mobile)
eric.althoff@novartis.com

Angela Fiorin
Novartis Global Pharma Communications
+41 61 324 8631 (direct)
+41 79 752 6955 (mobile)
angela.fiorin@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central
Samir Shah  +41 61 324 7944
Pierre-Michel Bringer  +41 61 324 1065
Thomas Hungerbuehler  +41 61 324 8425
Isabella Zinck  +41 61 324 7188

North America
Richard Pulik  +1 212 830 2448
Cory Twining  +1 212 830 2417