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FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER

PURSUANT TO RULE 13a-16 or 15d-16 OF

THE SECURITIES EXCHANGE ACT OF 1934

Report on Form 6-K dated September 19, 2016

(Commission File No. 1-15024)

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Novartis BAF312 reduces the risk of disability progression in pivotal phase III study in secondary progressive MS patients

EXPAND study data presented at ECTRIMS show that treatment with BAF312 (siponimod) reduced the risk of

- three-month confirmed disability progression by 21% vs placebo *in people with secondary progressive multiple sclerosis (SPMS)*

- SPMS is a progressive and highly disabling form of MS, and remains an area of significant unmet medical need

- Novartis continues to build on its experience and expertise in MS to advance care for people with the condition

Basel, September 17, 2016 - Novartis today announced positive results of the Phase III EXPAND study showing that oral once-daily BAF312 (siponimod) significantly reduced the risk of disability progression compared with placebo in people with secondary progressive multiple sclerosis (SPMS).[1] SPMS is a form of MS characterized by continuous worsening of neurological function over time, independent of relapses.[2] Topline results of EXPAND were presented at the 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), in London, UK.

BAF312 is a scientifically designed, selective sphingosine-1-phosphate (S1P) receptor modulator.[3] Initial data from the EXPAND study show:

- Treatment with BAF312 reduced the risk of three-month confirmed disability progression by 21% compared with placebo ($p=0.013$). The risk reduction for six-month confirmed disability progression was greater, further supporting robustness of the data.[1]

- A consistent reduction in the risk of confirmed disability progression across predefined subgroups, including patients without relapses.[1]

- A significant difference in favor of BAF312 compared to placebo in annualized relapse rate, the percent change in brain volume, and change from baseline in the volume of T2 lesions (brain lesions identified by a T2-weighted magnetic resonance imaging scan). Difference in change from baseline in the Timed 25-Foot Walk test (T25FW) was not significant.[1]

- BAF312 was generally safe and well tolerated, with a profile comparable to other drugs in the same class.[1]

"There are very few available treatment options to delay disease progression in SPMS, and there is a high unmet need for effective therapies with an acceptable safety profile for people with the condition," said Vasant Narasimhan, Global Head Drug Development and Chief Medical Officer for Novartis. "Novartis is the global leader in understanding the role of S1P receptor modulation in the treatment of MS, and the positive results of the EXPAND

study are a continuation of our ongoing efforts to innovate and meet the needs of patients. These data are a positive stride forward in an unserved disease area, and we look forward to evaluating next steps with health authorities."

EXPAND is the largest randomized, controlled study in secondary progressive multiple sclerosis to date.[4] Patients enrolled in EXPAND were representative of a general SPMS population.[1] They must have been diagnosed with SPMS and also demonstrated progression of disability in the two years prior to study.[1] The majority of patients had non-relapsing SPMS. The mean age at study entry was 48 years, and patients had a median Expanded Disability Status Scale (EDSS) score of 6.0, which corresponds to the use of walking aid.[1,5,6]

Novartis will complete full analyses of the EXPAND data and evaluate next steps in consultation with health authorities. The full study results, including data from primary and secondary endpoints, will be submitted for publication.

About the EXPAND study

The EXPAND study is a randomized, double-blind, placebo-controlled Phase III study, comparing the efficacy and safety of BAF312 versus placebo in people with secondary progressive multiple sclerosis (SPMS).[1,5] It is the largest randomized, controlled study in SPMS to date, and included 1,651 people with SPMS from 31 countries.[4] 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.[1] Patients had received a diagnosis of SPMS, and also demonstrated progression of disability in the two years prior to study.[1] 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 walking aid.[1,5,6] Patients were randomized to receive either 2mg BAF312 or placebo in a 2:1 ratio respectively.[1,5]

The primary endpoint of the study was the time to three-month confirmed disability progression, as measured by the EDSS, versus placebo.[1,5] Secondary endpoints included delay in the time to six-month confirmed disability progression versus placebo, the time to confirmed worsening of at least 20% from baseline in the timed 25-foot walk test (T25FW), T2 lesion volume, annualized relapse rate (ARR), and the safety and tolerability of BAF312 in people with SPMS.[1,5]

About BAF312 (siponimod)

BAF312 (siponimod) is a scientifically designed selective modulator of specific subtypes of the sphingosine-1-phosphate (S1P) receptor.[3] BAF312 binds to the S1P1 sub-receptor on lymphocytes and promotes their retention in lymphoid tissues, which prevents them from entering the central nervous system (CNS) of patients with multiple sclerosis (MS).[7,8] This leads to the anti-inflammatory effects of BAF312.[7,8]

The S1P receptor subtypes targeted by BAF312 are also found on the surface of cells in the CNS which play a role in the origin of secondary progressive MS (SPMS). BAF312 enters the CNS and by binding to these specific receptors, has the potential to modulate damaging cell activity and help to reduce the loss of neurological function associated with SPMS.[3, 9-11] The receptor specificity and pharmacokinetic properties (e.g. the faster elimination compared with first-generation S1P modulators) of BAF312 facilitate its ability to impact diseases such as SPMS, while improving its safety and convenience profile.[3]

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.[12] The evolution of MS results in an increasing loss of both physical (e.g. walking) and cognitive (e.g. memory) function.[13] There are three types of MS: relapsing remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS).[14]

SPMS is characterized by gradual worsening of neurological function over time.[2] This leads to a progressive accumulation of disability, independent of relapses, which can severely affect patients' abilities to carry out everyday activities.[2] It usually follows an initial phase of RRMS, which accounts for approximately 85% of all MS diagnoses; a quarter of people with RRMS will eventually go on to develop SPMS within 10 years of their initial RRMS diagnosis, rising to more than three-quarters after 30 years.[15,16] There remains a high unmet need for effective and safe treatments to help delay disability progression in SPMS.[17]

MS affects approximately 2.3 million people worldwide.[15]

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.

In addition to BAF312 (siponimod) in development in SPMS, investigational compounds include 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) 20mg/mL, the first generic version of Teva's Copaxone®* 20mg.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as "continues," "continuation," "ongoing efforts," "stride forward," "look forward," "next steps," "will," "in development," "investigational," "being investigated," or similar terms, or by express or implied discussions regarding potential marketing approvals for BAF312 and OMB157, potential new indications or labeling for Gilenya or Extavia, or regarding potential future revenues from BAF312, Gilenya, Extavia, OMB157 and Glatopa. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management 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 BAF312 or OMB157 will be approved for sale in any market, or at any particular time. Neither can there be any guarantee that Gilenya or Extavia will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that any of BAF312, Gilenya, Extavia, OMB157 or Glatopa will be commercially successful in the future. In particular, management's expectations regarding such products and investigational compounds could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected safety, quality or manufacturing issues, 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, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2015, the Group achieved net sales of USD 49.4 billion, while R&D throughout the Group amounted to approximately USD 8.9 billion (USD 8.7 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit <http://www.novartis.com>.

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References

- [1] Kappos L et al. Efficacy and safety of siponimod in secondary progressive multiple sclerosis - Results of the placebo controlled, double-blind, Phase III EXPAND study. Oral presentation presented at: 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis; September 14-17, 2016; London, UK.
- [2] MS Society. Secondary Progressive MS. <http://www.mssociety.org.uk/what-is-ms/types-of-ms/secondary-progressive-spms> (link is external). Accessed August 2016.
- [3] Gergely P et al. The selective sphingosine 1-phosphate receptor modulator BAF312 redirects lymphocyte distribution and has species-specific effects on heart rate. *Br J Pharmacol* 2012; 167(5):1035-47.
- [4] Kappos L et al. Baseline Subgroup Characteristics of EXPAND: A Phase 3 Study of Siponimod (BAF312) for the Treatment of Secondary Progressive Multiple Sclerosis (P3.084). *Neurology*. 2016; 86(16):suppl. P3.084
- [5] ClinicalTrials.gov. Exploring the Efficacy and Safety of Siponimod in Patients With Secondary Progressive Multiple Sclerosis (EXPAND). <https://clinicaltrials.gov/ct2/show/NCT01665144?term=BAF312+expand&rank=1> (link is external). Accessed July 2016.
- [6] MS Trust. Expanded Disability Status Scale. <https://www.mstrust.org.uk/a-z/expanded-disability-status-scale-edss> (Link is external). Accessed September 2016.
- [7] Brinkmann V, Billich A, Baumruker T, et al. Fingolimod (FTY720): discovery and development of an oral drug to treat multiple sclerosis. *Nat Rev Drug Discov* 2010; 9(11): 883-97.
- [8] Chun J, Hartung HP. Mechanism of action of oral fingolimod (FTY720) in multiple sclerosis. *Clin Neuropharmacol* 2010; 33(2): 91-101.
- [9] 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.
- [10] Brana C et al. Immunohistochemical detection of sphingosine-1-phosphate receptor 1 and 5 in human multiple sclerosis lesions. *Neuropathol Appl Neurobiol* 2014; 40(5): 564-78.
- [11] Tavares A et al. Brain distribution of MS565, an imaging analogue of siponimod (BAF312), in non-human primates. *Neurology* 2014; 82(10 (Suppl)): P1.168.
- [12] PubMed Health. Multiple Sclerosis. <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0024311/> (link is external). Accessed July 2016.
- [13] National Multiple Sclerosis Society. MS Symptoms. <http://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms> (link is external). Accessed July 2016
- [14] National Multiple Sclerosis Society. Types of MS. <http://www.nationalmssociety.org/What-is-MS/Types-of-MS> (link is external). Accessed August 2016.
- [15] Multiple Sclerosis International Federation. Atlas of MS 2013. <http://www.msif.org/wp-content/uploads/2014/09/Atlas-of-MS.pdf> (link is external). Accessed August 2016
- [16] Tremlett H, et al. The natural history of secondary-progressive multiple sclerosis. *Mult Scler*. 2008;14:314-324
- [17] Mehr S.R. and Zimmerman M.P. Reviewing the unmet needs of patients with multiple sclerosis. *Am Health Drug Benefits*. 2015; 8(6);426-431.

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Media Release (PDF): <http://hugin.info/134323/R/2042855/762570.pdf>

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Novartis AG

Date: September 19, 2016 By: /s/ PAUL PENEPEPENT
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Accounting