

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

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- -- EXPAND study data presented atECTRIMS 2016 show that treatment with BAF312 (siponimod) reduced the risk of three-month confirmed disability progression by 21% vs. placebo in patients with secondary progressive multiple sclerosis (SPMS)
- -- SPMS is a progressive and highly disabling form of MS and there are no approved treatments currently available in the US
- -- Novartis continues to build on its experience and expertise in MS to advance care for people with SPMS

EAST HANOVER, N.J., Sept. 17, 2016 /PRNewswire/ -- Novartis today announced positive results of the Phase III EXPAND study showing that oral once-daily BAF312 (siponimod) significantly reduced the risk of confirmed disability progression compared with placebo in people with secondary progressive multiple sclerosis (SPMS). SPMS is a form of MS characterized by continuous worsening of neurological function over time, independent of relapses. 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 an investigational selective sphingosine-1-phosphate (S1P) receptor modulator. Initial, first interpretable 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.
- A consistent reduction in the risk of three-month confirmed disability progression across predefined subgroups.
- A significant difference in favor of BAF312 compared to placebo over 12 and 24 months 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). The difference in change from baseline in the timed 25-foot walk test (T25FW) was not significant.
- BAF312 was generally safe and well tolerated, with a profile comparable to other drugs in the same class.

"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 of 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 SPMS to date. Patients enrolled in EXPAND were

representative of a general SPMS population. They must have been diagnosed with SPMS and also demonstrated progression of disability in the two years prior to study. 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 a walking aid.

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 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 walking aid. Patients were randomized to receive either 2mg BAF312 or placebo in a 2:1 ratio, respectively.

The primary endpoint of the study was the time to three-month confirmed disability progression, as measured by the EDSS, versus placebo. Secondary endpoints included delay in the time to six-month confirmed disability progression based on EDSS 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.

About BAF312 (siponimod)

BAF312 (siponimod) is an investigational selective modulator of specific types of the sphingosine-1-phosphate (S1P) receptor. The S1P receptor is commonly found on the surface of specific cells residing in the central nervous system (CNS), that are responsible for causing CNS damage that drives loss of function in secondary progressive MS (SPMS). In-vitro studies show that BAF312 enters the brain and by binding to these specific receptors, may prevent the activation of these harmful cells, helping to reduce loss of physical and cognitive function associated with SPMS.

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 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, independent of relapses, which can severely affect patients' abilities to carry out everyday activities. 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. There remains a high unmet need for effective and safe treatments to help delay disability progression in SPMS.

MS affects around 400,000 people in the US.

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," "investigational," "continuation," "ongoing efforts," "stride forward," "look forward," "next steps," "will," "in development," "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 Pharmaceuticals Corporation offers a broad range of medicines for cancer, cardiovascular disease, endocrine disease, inflammatory disease, infectious disease, neurological disease, organ transplantation, psychiatric disease, respiratory disease and skin conditions.

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which 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

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