Phase III data in The Lancet show Novartis siponimod significantly improved outcomes in patients with secondary progressive MS

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- -- EXPAND shows oral siponimod (BAF312) is the first investigational disease-modifying therapy in a large trial that meaningfully delayed disability progression in typical secondary progressive MS (SPMS) patients(1)
- -- Results demonstrate siponimod also had beneficial effects on clinical relapses and MRI disease activity, including brain volume loss(1)
- -- Novartis plans to file siponimod for US approval in SPMS in early 2018

EAST HANOVER, N.J., March 22, 2018 /PRNewswire/ -- Novartis today announced that the full results from the Phase III EXPAND study of oral, once-daily siponimod (BAF312) in secondary progressive multiple sclerosis (SPMS) were published in the peer-reviewed journal The Lancet. These pivotal results show siponimod significantly reduced the risk of three-month confirmed disability progression versus placebo (primary endpoint)[1]. Siponimod also meaningfully delayed the risk of six-month confirmed disability progression and demonstrated favorable outcomes in other relevant measures of multiple sclerosis (MS) disease activity[1]. If approved, siponimod would be the first disease-modifying therapy to delay disability progression in a large trial of typical SPMS patients, including many who had reached a non-relapsing stage and high level of disability[1].

SPMS is a form of MS that is associated with progressive, irreversible physical and cognitive disability, largely independent of relapses[2]. Patients transition to SPMS after an initial phase of relapsing-remitting MS (RRMS), the most commonly diagnosed type of MS[3,4]. There is a high unmet medical need for new treatments that are safe and effective for patients with SPMS[5].

"Today's published full EXPAND results show that siponimod can delay disability progression in typical established SPMS patients, where other approaches tested so far have been unsuccessful," said Professor Ludwig Kappos, University Hospital Basel and Principal Investigator of EXPAND. "These data are all the more impressive when considering that the majority of patients had already advanced disability when starting treatment in EXPAND."

Siponimod is an investigational selective modulator of specific subtypes of the sphingosine-1-phosphate (S1P) receptor[6]. Full data from EXPAND show that siponimod reduced the risk of three-month confirmed disability progression by a statistically significant 21% versus placebo (p=0.013); efficacy was overall consistent across pre-defined patient subgroups[1]. Other clinically relevant endpoint data show that siponimod, when compared to placebo:

- Did not show a significant difference in the Timed 25-Foot Walk test, the first key secondary endpoint, and the MS Walking Scale[1]
- Limited the increase of T2 lesion volume by approximately 80%, measured by volume change from

baseline (mean over 12 and 24 months, p<0.0001), the second key secondary endpoint[1]
- Reduced the risk of six-month confirmed disability progression by 26% (p=0.0058)[1]
- Reduced annualized relapse rate (ARR) by 55% (p<0.0001)[1]
- Slowed the rate of brain volume loss by 23% (relative difference; mean across 12 and 24 months, p=0.0002)[1]
- Demonstrated a safety profile which was overall consistent with the known effects of S1P receptor modulation[1]

"Novartis is dedicated to advancing MS research and pioneering solutions for people living with SPMS - a complex, debilitating disease," said Danny Bar-Zohar, Global Head Neuroscience Development, for Novartis. "The pivotal EXPAND data provide patients, and the medical community alike, with hope that a much needed, safe and effective treatment option is on the horizon for SPMS, for which treatment options are scarce. We look forward to continuing to work with regulatory agencies to make siponimod available for these patients as fast as possible."

Novartis plans to file for regulatory approval of siponimod for SPMS with the US Food and Drug Administration in early 2018. The EXPAND results have previously been presented at scientific congresses.

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 SPMS[1,7]. It is the largest randomized, controlled study in SPMS to date, and included 1,651 people with SPMS from 31 countries[1,8]. At the time of the study, individuals enrolled in EXPAND had a mean age of 48 years and the mean times since first MS symptoms and conversion to SPMS were 17.1 (±8.4) and 3.9 (±3.6) years for siponimod and 16.2 (±8.2) and 3.6 (±3.3) years for placebo, respectively[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 unilateral walking aid (e.g., a cane or a crutch)[1,7]. Patients were randomized to receive either 2mg siponimod once-daily or placebo, in a 2:1 ratio[1,7]. Patients continued on siponimod treatment in the open-label long-term extension part of the study[1].

About Siponimod (BAF312)

Siponimod is an investigational selective modulator of specific subtypes of the sphingosine-1-phosphate (S1P) receptor[6]. 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 SPMS.

About Multiple Sclerosis

MS is a chronic disorder of the CNS that disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss[9]. 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), SPMS and primary progressive MS (PPMS)[4].

SPMS is characterized by gradual worsening of neurological function over time[2]. This leads to a progressive accumulation of disability, largely independent of relapses, which can severely affect patients' abilities to carry out everyday activities[2]. It 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[3,10]. There remains a high unmet need for effective and safe treatments to help delay disability progression in SPMS[5].

MS affects around 400,000 people in the US[11].

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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 122,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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