Novartis provides update on fingolimod Phase III trial in primary progressive MS (PPMS)

- Phase III study in primary progressive multiple sclerosis (PPMS) did not meet the primary endpoint
- PPMS is distinct from other types of MS, with no approved treatment that can change the course of this devastating disease
- Novartis remains strongly committed to identifying and developing treatment options for patients with chronic debilitating neurological conditions

Basel, Dec 1, 2014 – Novartis announced today that the Phase III INFORMS study in primary progressive multiple sclerosis (PPMS) did not show a significant difference between fingolimod and placebo on a combination of disability measures. The safety results were consistent with the well-characterized safety profile of fingolimod in relapsing MS (RMS).

PPMS is a disorder of the central nervous system (CNS) which affects approximately 10% of the 2.3 million patients diagnosed with MS worldwide. PPMS is a distinct disease form, different from relapsing MS in terms of its basic disease process, near-absence of acute relapses and fewer active MRI lesions. The severe irreversible damage to the CNS in PPMS is thought to be caused by different pathways leading to loss of nerve cells and a more rapid, continuous loss of function over time which profoundly impacts patients' lives. Additionally, the disease is typically diagnosed later than other types of MS, when significant damage to the CNS has already occurred. Despite considerable research and academic focus, there are currently no approved treatments that have been shown to change the course of this debilitating disease and management focuses mainly on the treatment of symptoms.

"We understand this news is very disappointing for those affected by PPMS and involved in its management. While PPMS is a focus of the MS community, relatively little is known about the disease so finding effective treatments remains a challenge. We will actively work with the MS community to review and analyze the INFORMS results to help increase the understanding of this devastating disease," said Vasant Narasimhan, Global Head of Development at Novartis Pharmaceuticals. "Gilenya (fingolimod) revolutionized the treatment of relapsing MS as the first oral disease-modifying therapy. We remain strongly committed to continuing to research new treatment options for patients with MS and other neurological conditions."

The INFORMS study was based on the knowledge that fingolimod enters the central nervous system (CNS) and can interact with damage-causing cells residing in the CNS. It was hypothesized that this central effect, which is well understood in relapsing forms of MS, would also be relevant in PPMS. As opposed to the consistently strong efficacy seen in relapsing MS, the results of the INFORMS study seem to suggest that PPMS and relapsing forms of MS have different underlying mechanisms.
Fingolimod, marketed as Gilenya®, is approved in the US for first-line treatment of relapsing forms of MS in adults⁸. In the EU, Gilenya is indicated for adult patients with highly active relapsing-remitting MS (RRMS) defined as either high disease activity despite treatment with at least one disease-modifying therapy (DMT), or rapidly evolving severe RRMS⁹. Gilenya is the only DMT to impact the course of relapsing MS with high efficacy across four key measures of disease activity: relapses, MRI lesions, brain shrinkage (brain volume loss) and disability progression¹⁰⁻¹⁴. The likelihood of achieving ‘no evidence of disease activity’ (NEDA) across four key measures is more than four-times greater in relapsing MS patients treated with Gilenya compared to placebo¹⁵. The safety profile of Gilenya in RMS is well understood and based on substantial evidence from three major clinical trials and extensive real-world experience in more than 100,000 patients, with the total patient exposure now at approximately 172,500 patient years.

About INFORMS
The INFORMS study is a double-blind, randomized, multi-center, placebo-controlled parallel group study, comparing the efficacy and safety of fingolimod (0.5 mg) versus placebo in people with primary progressive multiple sclerosis (PPMS)¹⁶. The INFORMS study is the largest clinical trial ever conducted in PPMS. Nine-hundred and seventy (970) people aged 25-69 years with PPMS were enrolled in INFORMS from 148 sites, across 18 countries, including Australia, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Hungary, Italy, Netherlands, Poland, Spain, Sweden, Switzerland, Turkey, UK and the US. Patients were treated for at least three years¹.

The primary endpoint was to evaluate the effect of fingolimod versus placebo on reducing the risk of three-month sustained disability progression based on a composite measure of Expanded Disability Status Scale (EDSS), assessment of upper limb function (9-Hole Peg Test, HPT), and walking speed (25-foot Timed Walk Test, TWT)¹.

About Gilenya (fingolimod)
In relapsing MS, the loss of physical and cognitive function is driven by two types of damage that result in the loss of neurons and brain tissue – distinct inflammatory lesions (referred to as focal damage), and more widespread inflammatory neurodegenerative processes (referred to as diffuse damage). Focal damage results in the loss of brain tissue and can clinically present as relapses. Diffuse damage starts early in the disease, often goes unnoticed and is also associated with loss of brain tissue and accumulated loss of function¹⁷⁻¹⁹.

Gilenya (fingolimod) targets both focal and diffuse central nervous system (CNS) damage that drive loss of function in relapsing MS. It prevents cells that cause focal inflammation from reaching the brain (referred to as ‘peripheral’ action), but also enters the CNS and reduces the diffuse damage by preventing the activation of harmful cells residing in the CNS (referred to as ‘central action’)²⁻⁷. It is important to address both focal and diffuse damage in relapsing MS to effectively impact disease activity and help preserve an individual’s physical (e.g. walking) and cognitive (e.g. memory) function.

Phase III studies with fingolimod are currently being conducted in two rare diseases, pediatric MS and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), where there is a high unmet need.

About Novartis in Multiple Sclerosis
Novartis is committed to the research and development of innovative and targeted treatment options for people suffering from different types of MS.

The Novartis MS portfolio includes Gilenya (fingolimod, oral DMT) and Extavia® (interferon beta-1b for subcutaneous injection) for the treatment of relapsing MS. In addition to the current clinical development program with Gilenya, Novartis is investigating BAF312 (siponimod), a second generation, selective S1P1 and 5 receptor
modulator, in the largest Phase III trial in secondary progressive MS (SPMS). The IL-17 pathway is also being explored as a novel therapeutic target in MS.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as “committed,” “will,” “suggest,” “being conducted,” “being explored,” or similar terms, or by express or implied discussions regarding potential future indications or labeling for Gilenya, potential future marketing submissions or approvals for the other investigational compounds in the Novartis MS portfolio, or regarding potential future revenues from any or all of the products and investigational compounds in the Novartis MS portfolio, including Gilenya. 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 Gilenya will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Neither can there be any guarantee that any of the investigational compounds in the Novartis MS portfolio will be submitted or approved for sale in any market, or at any particular time. Nor can there be any guarantee that any of the products and investigational compounds in the Novartis MS portfolio will be commercially successful in the future. In particular, management’s expectations regarding these products 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 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, cost-saving generic pharmaceuticals, preventive vaccines, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2013, the Group achieved net sales of USD 57.9 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 133,000 full-time-equivalent associates and sell products in more than 150 countries around the world. For more information, please visit http://www.novartis.com.

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