Long-term efficacy of Gilenya® reinforced by new ‘no evidence of disease activity’ (NEDA-4) analysis in MS patients over seven years

- **NEDA-4** – no evidence of disease activity based on four parameters – relapses, MRI lesions, brain shrinkage and disability progression – is a comprehensive measure of MS disease control
- 31.2% to 44.8% of patients continuously treated with Gilenya in the FREEDOMS core and extension trials achieved NEDA-4 in each of the years three to seven
- Separate analysis confirmed NEDA-4 status in the first year is a better predictor of long-term outcomes than an assessment of three parameters (relapses, MRI lesions and disability progression)

**Basel, October 8, 2015** – Novartis announced today a new analysis from the phase III FREEDOMS and FREEDOMS II trials reinforcing the long-term efficacy profile of Gilenya® (fingolimod). The analysis evaluated the proportion of Gilenya patients with relapsing multiple sclerosis (RMS) achieving ‘no evidence of disease activity’ (NEDA-4) every year over seven years. NEDA-4 is achieved when a patient has no relapses, MRI lesions, MS-related brain shrinkage and disability progression. These data were presented at the 31st Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in Barcelona, Spain.

This follow-up analysis of pooled data from the FREEDOMS and FREEDOMS II core and extension trials was conducted to assess NEDA-4 each year for seven years in patients with RMS. The data showed that in the first year, 27.1% of patients on Gilenya achieved NEDA-4 compared to 9.1% on placebo. Switching from placebo to Gilenya after year two doubled the proportion of patients achieving NEDA-4 (12.7% to 27.4%) in year three. Of those patients on continuous Gilenya treatment, 31.2% to 44.8% had NEDA-4 status in each of the years three to seven.

“MS is a chronic debilitating disease and these data are important in showing the long-term efficacy of Gilenya, and the importance of early treatment to help improve long-term outcomes for patients,” said Vas Narasimhan, Novartis Global Head of Development. “Better understanding of the course of a person’s MS through assessment of NEDA-4 can help physicians identify the optimal, effective treatment approach as early as possible for their patients.”

A separate follow-up analysis of data from the FREEDOMS and FREEDOMS II trials also confirmed for the first time that assessment of RMS based on NEDA-4 allowed physicians to better predict long-term disability and brain shrinkage outcomes than just assessing relapses, MRI lesions and disability progression. NEDA-4 status over the first year was a significantly better predictor of disability and brain shrinkage over the subsequent five years, as measured by patients reaching a stage of severe disability (EDSS ≥6: patients require a crutch to walk approximately 100m) (p<0.0127) or having more than 0.4% mean annual brain volume loss. These findings support the importance...
of assessing RMS with NEDA-4 to enable a more reliable prediction of long-term disease outcomes.

### About Multiple Sclerosis

Multiple sclerosis (MS) is a chronic disorder of the central nervous system 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 and cognitive (e.g. memory) function. This has a substantial negative impact on the approximately 2.3 million people worldwide affected by MS, a disease that most often begins in early adulthood.

People with MS can be diagnosed with relapsing forms of MS (RMS), which include relapsing remitting MS and secondary progressive MS, or with primary progressive MS.

The loss of physical and cognitive function in RMS 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 function.

### About Gilenya

Gilenya is the only oral disease-modifying therapy (DMT) to impact the course of relapsing MS (RMS) with high efficacy across four key measures of disease activity: relapses, MRI lesions, brain shrinkage (brain volume loss) and disability progression. It is approved in the US for the first-line treatment of relapsing forms of MS in adults and in the EU for adult patients with highly-active relapsing remitting MS (RRMS) defined as either high disease activity despite treatment with at least one DMT, or rapidly-evolving severe RRMS.

Gilenya targets both focal and diffuse central nervous system (CNS) damage. 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’). It is important to address both focal and diffuse damage in RMS to effectively impact disease activity and help preserve an individual’s functions.

Gilenya has been used to treat approximately 125,000 patients in both clinical trials and the post-marketing setting, with more than 240,000 years of patient experience. The overall benefit risk profile of Gilenya remains positive.

### About Novartis in Multiple Sclerosis

The Novartis multiple sclerosis (MS) portfolio includes Gilenya, which is indicated for relapsing forms of MS and also in development for pediatric MS and chronic inflammatory demyelinating polyneuropathy (CIDP). 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 BAF312, currently in phase III clinical development and being investigated as an oral therapy for SPMS. Novartis is also exploring the IL-17 pathway in MS with CJM112.

Novartis also recently announced an agreement to acquire all remaining rights to GlaxoSmithKline’s Ofatumumab, a fully human monoclonal antibody in development for
RRMS. Ofatumumab targets CD20, and is ready to begin phase III pivotal studies. This agreement is subject to customary closing requirements and approval by the US Federal Trade Commission.

Additionally, in the US the Sandoz Division of Novartis markets Glatopa™, 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 "long-term," "can," "predict," "prediction," "investigational," "development," "being investigated," "exploring," "ready," or similar terms, or by express or implied discussions regarding potential new indications or labeling for Gilenya, potential future marketing approvals for compounds in development, or regarding potential future revenues from such products or from Extavia. 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. Nor can there be any guarantee that any compounds in development will be submitted or approved for sale in any market, or at any particular time. Neither can there be any guarantee that any of these products, including Extavia, will be commercially successful in the future. In particular, management's expectations regarding such 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 and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2014, the Group achieved net sales of USD 58.0 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 120,000 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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