Novartis in Multiple Sclerosis Media Fact Sheet

Our expertise
For more than 50 years, Novartis has made significant advances in neuroscience, changing the way we treat disorders of the central nervous system (CNS). Novartis has pioneered early breakthrough treatments for many neurological and psychiatric conditions, some of which remain important treatments to this day.

Our commitment
The Novartis pipeline has been ranked as one of the strongest and includes products that may provide benefit in the future for those with neurological disorders including multiple sclerosis (MS).

Novartis is committed to working with the community to provide advanced therapeutics and novel solutions to people living with MS. Novartis seeks to develop therapies and programs that address all aspects of health by understanding the needs of people with MS and their healthcare providers.

By combining passion and energy with our extensive neurology experience, Novartis looks to the future of MS treatment with a fresh attitude.

Our portfolio
Gilenya® (fingolimod)
- Gilenya (fingolimod) is the first in a new class of compounds called sphingosine 1-phosphate receptor (S1PR) modulators and the first oral therapy approved to treat relapsing forms of MS.
- Gilenya is a generally highly effective once-daily oral MS treatment without label restrictions specific to treatment duration. In clinical trials Gilenya was generally well-tolerated with a manageable safety profile.
- Gilenya was approved based on the largest phase III clinical trial program in MS at the time of submission, including data showing significant efficacy in reducing relapses, the risk of disability progression, and the number of brain lesions detected by magnetic resonance imaging (MRI), a measure of disease activity in people with MS.
  - In a pivotal phase III clinical trial, Gilenya treatment demonstrated superior efficacy to interferon beta-1a IM (Avonex®), a commonly prescribed treatment, reducing relapses by 52% (p<0.001) at one year (TRANSFORMS).
  - In a post-hoc analysis, Gilenya showed a 61% relative reduction in annualized relapse rate (ARR) compared to interferon beta-1a IM at one year in subgroups of patients with highly active relapsing-remitting MS (RRMS) not responding to interferon treatment (p<0.001).
- Results from the phase III FREEDOMS extension study showed improvements in clinical and MRI measures in patients who switched from placebo (administered during the 24-month core study) to Gilenya (administered during the extension).
  - Patients who switched from placebo to Gilenya saw a 55% decrease in their annualized relapse rate (ARR) during the extension phase compared to the core phase (ARR [core] = 0.29 vs. ARR [extension] 0.13; p<0.001).
  - Significantly more patients on continuous fingolimod treatment compared to those first randomized to placebo remained relapse-free (59% vs. 37%) and free from three-month confirmed disability progression (74 % vs. 66 %).
- Gilenya is now approved in 70 countries.
- Currently more than 63,000 patients have been treated in clinical trials and in a post-marketing setting, and there are approximately 73,000 patient years of exposure.
- In phase II and III clinical and extension studies, Gilenya was generally well tolerated with a manageable safety profile. The most common side effects were headache, liver enzyme elevations, influenza, diarrhea, back pain, and cough. Other Gilenya-related side effects include transient, generally asymptomatic, heart rate reduction and atrioventricular block upon treatment initiation, mild blood pressure increase, macular edema, and mild bronchoconstriction.

Extavia®
- Extavia is a Novartis branded interferon beta-1b, indicated for early and more advanced forms of MS including relapsing-remitting and secondary-progressive MS with relapses (EU only).
  - Interferon beta-1b is believed to work by modulating the immune system to reduce inflammatory damage.
Extavia provides patients and physicians with an additional option when prescribing the mainstay of care for MS.

Extavia was launched in several EU countries in early 2009. This marked the beginning of a long-term commitment with the MS community and laid the foundations for future innovations in MS therapy.

**BAF312 (siponimod)**

- BAF312 (siponimod) is an investigational compound in the Novartis MS portfolio. BAF312 is an oral selective modulator of the sphingosine 1-phosphate (S1P) molecules receptor subtypes 1 and 5 (S1P1, 5R modulator) with a fast washout (6 days).
- BAF312 was designed to have a short half-life (150 hour based on a 30 hour half-life), which provides a rapid recovery of blood lymphocyte counts following treatment discontinuation.
- Novartis will initiate a phase III program to investigate BAF312 as a treatment option for secondary-progressive multiple sclerosis (SPMS). SPMS is a type of MS where there are currently limited treatments options and of the 85% of people initially diagnosed with relapsing-remitting MS (the most common form of the disease), approximately half will transition to SPMS within 10 years and 90% will transition within 25 years.
- The phase III EXPAND (Exploring the Efficacy and Safety of Siponimod in Patients with Secondary Progressive Multiple Sclerosis) study is a multinational, randomized, double-blind parallel-group placebo-controlled variable treatment duration study in 1530 patients with SPMS. The primary endpoint of the EXPAND study is to demonstrate the efficacy of BAF312 in delaying the time to 3-month confirmed disability progression of SPMS, as measured by Expanded Disability Status Scale (EDSS), relative to placebo.
- Results from the phase II BOLD (BAF312 On MRI Lesion given once Daily) study demonstrated a statistically significant (p=0.0001) dose response relationship among five doses of BAF312 and placebo during three months of treatment in patients with RRMS, as measured by the number of combined unique active MRI lesions (CUAL):
  - At 3 months the dose-response relationship for BAF312 was significant (p=0.0001); BAF312 reduced CUAL by up to 80% compared to placebo, with doses of BAF312 10 and 2 mg forming the upper plateau of the dose-response curve.
- In Phase II BOLD study, BAF312 demonstrated a favorable safety and tolerability profile when an initial dose titration regimen was used at the start of treatment. The most common adverse events were headache, bradycardia, dizziness and nasopharyngitis.
- The ongoing clinical development for BAF312 demonstrates the continued Novartis commitment to developing a robust portfolio of therapeutic options for the MS community that address unmet patient needs across the disease continuum.

**AIN457 (secukinumab)**

- AIN457 (secukinumab) is a recombinant fully human anti-human interleukin-17A (IL-17A) monoclonal antibody that binds to and neutralizes the bioactivity of human IL-17A.
- Preclinical and human evidence have implicated IL-17 in the pathogenesis of RRMS.
- The first AIN457 positive proof of concept study in relapsing–remitting MS was presented as a late breaking oral presentation at ECTRIMS 2012.

**References**

7. Gergely et al. The selective S1P receptor modulator BAF312 redirects lymphocyte distribution and has species-specific effects on heart rate: translation from preclinical to clinical studies. BJPharmacol, May 30 2012.