

NOVARTIS AG  
Form 6-K  
April 20, 2012

# SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

## FORM 6-K

**REPORT OF FOREIGN PRIVATE ISSUER  
PURSUANT TO RULE 13a-16 or 15d-16 OF  
THE SECURITIES EXCHANGE ACT OF 1934**

Report on Form 6-K dated April 19, 2012

(Commission File No. 1-15024)

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(Name of Registrant)

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(Address of Principal Executive Offices)

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**MEDIA RELEASE • MEDIA RELEASE • MEDIA RELEASE**

**New extension study data with Novartis drug Gilenya® shows patients successfully treated for up to 7 years in relapsing MS**

- *Results from open label phase III extension and 7-year phase II extension studies show sustained low disease activity on clinical and MRI measures in patients continuing on Gilenya (fingolimod) treatment*
- *Extension study results demonstrate a safety profile for Gilenya consistent with pivotal trials*
- *Data from FIRST study in more than 2,400 patients show overall low incidence of first dose bradycardia and conduction abnormalities at treatment initiation with Gilenya*
- *New findings from phase IIb trial for investigational compound BAF312 (siponimod) show positive outcomes for MS patients*

**Basel, April 19, 2012** New data will be presented at the 64th annual meeting of the American Academy of Neurology (AAN) that support the efficacy and safety profile of Gilenya® (fingolimod), the only oral therapy approved to treat relapsing forms of multiple sclerosis (MS)(1),(2). Novartis will also showcase new data on its investigational compound BAF312 (siponimod), a selective modulator of the S1P receptor subtypes 1 and 5 (S1P1, -5R modulator) in its multiple sclerosis portfolio(3).

The data being presented reinforce our confidence in the sustained efficacy and safety profile of Gilenya said David Epstein, Head of the Pharmaceuticals Division of Novartis Pharma AG. We also are pleased to present encouraging data for our investigational compound BAF312 (siponimod). The clinical development of BAF312 demonstrates our commitment to developing new therapeutic options for the MS community.

**New data presented on long-term efficacy and safety profile of Gilenya**

New results from the phase III FREEDOMS extension study showed significant 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). 1033 patients completed the two-year, double-blind FREEDOMS 24 month core study. Of these, 90% of patients completed 3 years observation and 45% were followed for 4 years in this study before being transferred to the umbrella follow-up study (LONGTERMS). 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%). MRI measures continued to show significant effects in favor of fingolimod treatment, including a significantly reduced rate of brain atrophy in the patients treated continuously as compared to switch patients (mean (%) change in brain volume -1.67% vs. -2.24%;  $p = 0.001$ )(1) at the end of the observation. In the core FREEDOMS study, Gilenya reduced the rate of brain atrophy by 38% versus placebo at two years (0-24 months)(4).

The phase III FREEDOMS extension showed a safety profile consistent with that of the pivotal phase III trials(1). The most common adverse events were nasopharyngitis, low lymphocyte counts (to be expected from the mode of action), upper respiratory tract infections and influenza(4)-(5).

This extension study confirms the efficacy shown in the published phase III studies and supports the positive long term impact of continuous treatment. The favorable longer term safety profile is consistent with results from the phase III studies, said Ludwig Kappos, Department of Neurology, University of Basel, Switzerland. These observations in a large group of patients, now for four and more years, confirm that fingolimod is a valuable treatment option for patients with relapsing remitting MS.

Additionally, new data for up to 7 years of treatment from the phase II extension study demonstrated patients treated with Gilenya (n=122) had sustained low MRI and clinical disease activity(2). The overall ARR for the continuous Gilenya treatment group was 0.16, which can be expressed as one relapse every 6 years. Of patients on continuous Gilenya treatment since study start and who completed the long-term extension, over half had remained free of relapses throughout the study(2).

The phase III registration program for Gilenya included the two-year FREEDOMS study and a head-to-head study in which Gilenya showed a 52% relative reduction in annualized relapse rate (primary endpoint) compared to Avonex® (interferon-beta-1a IM), a commonly prescribed treatment, at one year(5).

#### **Low incidence of ECG abnormalities and symptomatic heart rate reduction at treatment initiation in 2,400 patient FIRST Study**

New data from the large, 4-month, open-label, single-arm multi-center FIRST study demonstrate an overall low incidence of significant first dose bradycardia [i.e. 1.3% of patients experienced bradycardia < 45 bpm and no patient experienced a heart rate <30 bpm] and conduction abnormalities at treatment initiation with Gilenya(6). Importantly, this study provides data on continuous ECG monitoring by ambulatory Holter Electrocardiogram (ECG) for six hours following the administration of the first dose to identify any heart rate or ECG abnormalities. Results from more than 2,400 patients showed the incidence of Mobitz I second degree atrioventricular blocks (AVBs) was 1.4% at the post-dose Holter ECG for 6 hours after administration, and the incidence of Mobitz II second degree, or 2:1 AVBs was 0.5%. The short-term safety profile of Gilenya in the FIRST study was generally consistent with that observed in the phase III studies. This included the low incidence of the known cardiac effects of fingolimod at treatment initiation (typically transient decreases in heart rate and generally asymptomatic atrioventricular blocks).

#### **Positive phase IIb data for BAF312 (siponimod)**

Novartis will also present the key results from a phase II dose finding study of its investigational compound BAF312 (siponimod), a selective modulator of the S1P receptor subtypes 1 and 5 (S1P1, 5-R modulator), in MS. This double-blind placebo-controlled study applied an innovative adaptive trial design to optimally describe the dose response relationship. A statistically significant dose response relationship could be established. Further, the study showed that treatment with BAF312, when compared to placebo, reduced brain MRI lesions up to 80%(3). Relapses were infrequent and appeared reduced with treatment (ARR for 2 mg 0.20 vs. placebo 0.58;  $p=0.044$ ). Data also showed that BAF312 was generally well-tolerated with an initial dose titration. The most frequent adverse events were headache, bradycardia, dizziness and nasopharyngitis (3). A phase III MS program is planned to start later this year.

**About Gilenya**

Gilenya, licensed from Mitsubishi Tanabe Pharma Corporation, is the first in a new class of compounds called sphingosine 1-phosphate receptor (S1PR) modulators. It has

demonstrated superior efficacy compared to Avonex, a commonly prescribed treatment, showing a 52% relative reduction in annualized relapse rate (primary endpoint) and a 40% relative reduction in the rate of brain atrophy (secondary endpoint) at one year in a pivotal head-to-head trial in patients with relapsing-remitting multiple sclerosis(4). In a recent sub-analysis, Gilenya showed a 61% relative reduction in annualized relapse rate compared to interferon-beta-1a (IM) at one year in subgroups of patients with highly active relapsing-remitting MS not responding to interferon treatment(7).

Gilenya is generally a highly effective once-daily oral MS treatment. In clinical trials it was generally well tolerated with a manageable safety profile, and there is increasing experience of Gilenya's long-term effectiveness and safety profile, with approximately 36,000 patients having been treated in clinical trials and in a post-marketing setting(8). Currently, there is approximately 34,000 patient years of exposure. In clinical trials, the most common side effects were headache, liver enzyme elevations, influenza, diarrhea, back pain, and cough. Other Gilenya-related side effects included transient, generally asymptomatic, heart rate reduction and atrioventricular block upon treatment initiation, mild blood pressure increase, macular edema, and mild bronchoconstriction(4),(5).

The rates of infections overall, including serious infections, were comparable among treatment groups, although a slight increase in lower respiratory tract infections (primarily bronchitis) was seen in patients treated with Gilenya. The number of malignancies reported across the clinical trial program was small, with comparable rates between the Gilenya and control groups(4),(5).

#### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as will, encouraging, commitment, planned, or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Gilenya, potential future marketing approvals for BAF312, or regarding potential future revenues from Gilenya or BAF312. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Gilenya will be approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that BAF312 will be submitted for approval, or approved for sale, in any market or at any particular time. Neither can there be any guarantee that either Gilenya or BAF312 will achieve any particular levels of revenue in the future. In particular, management's expectations could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; competition in general; government, industry and general public pricing pressures; unexpected manufacturing issues; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; the impact that the foregoing factors could have on the values attributed to the Novartis Group's assets and liabilities as recorded in the Group's consolidated balance sheet, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. 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 and diagnostic tools, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2011, the Group's continuing operations achieved net sales of USD 58.6 billion, while approximately USD 9.6 billion (USD 9.2 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Novartis Group companies employ approximately 124,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit <http://www.novartis.com>.

Novartis is on Twitter. Sign up to follow @Novartis at <http://twitter.com/novartis>.

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- (2) Antel J. et al. Long-term (7-Year) Data from A Phase 2 Extension Study of Fingolimod in Relapsing Multiple Sclerosis. Poster Presentation at AAN, New Orleans, April 2012.
- (3) Stüve O. et al. BAF312, a Selective Sphingosine-1-Phosphate Receptor Modulator Improves MRI and Clinical Outcomes in Relapsing-Remitting Multiple Sclerosis (RRMS). Platform Presentation at AAN, New Orleans, April 2012.
- (4) Kappos L, et al. Placebo-Controlled Study of Oral Fingolimod in Relapsing Multiple Sclerosis. *N Eng J Med*. Vol.362 No.5, Feb 4, 2010; 362:387-401.
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- (7) Havrdová E. et al. Clinical outcomes in subgroups of patients with highly action relapsing-remitting multiple sclerosis treated with Fingolimod (FTY720): Results from the FREEDOMS and TRANSFORMS phase III studies. Poster presented atECTRIMS, Amsterdam, October 2011.
- (8) Data on file.

Avonex® is a registered trademark of Biogen Idec.

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**Novartis AG**

Date: April 19, 2012

By: /s/ MALCOLM B. CHEETHAM

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Reporting and Accounting