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

Apr 24, 2012

- 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 cardiac conduction abnormalities at Gilenya treatment initiation
- New findings from phase IIb trial for investigational compound BAF312 (siponimod) show positive outcomes for MS patients

East Hanover, NJ, April 23, 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, 5-R 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 (siponimod) 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). A total of 1033 patients completed the two-year, double-blind, placebo-controlled FREEDOMS core study. Approximately, 90% of patients completed a total of 3 years in the study 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 Gilenya treatment compared to those first randomized to placebo remained relapse-free (59% vs 37%). In addition, an increased proportion of continuously treated Gilenya patients did not demonstrate three-month confirmed disability progression compared to the switch group (74% vs 66%). MRI measures continued to show significant effects in favor of Gilenya treatment.

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

Additionally, new data from the phase II extension study (n=122 completers) demonstrated patients treated

with Gilenya had sustained low MRI and clinical disease activity for up to 7 years. 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 pivotal trial program for Gilenya included the two-year, placebo-controlled FREEDOMS study, which showed 54% relative reduction ARR versus placebo and a one-year head-to-head TRANSFORMS study in which Gilenya showed a 52% relative reduction in ARR (primary endpoint) compared to Avonex® (interferon-beta-1a IM), a commonly prescribed treatment.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 first dose bradycardia and cardiac 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 Gilenya at treatment initiation (typically transient decreases in heart rate and generally asymptomatic AVBs).

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 relapsing-remitting MS. This double-blind, placebo-controlled, study applied an innovative adaptive trial design to effectively 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 the number of brain MRI lesions up to 80%.3 Relapses were infrequent and 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™ (fingolimod)
Gilenya, licensed from Mitsubishi Tanabe Pharma Corporation, is the first in a new class of drugs called sphingosine 1-phosphate receptor (S1PR) modulators. Gilenya works by targeting S1P receptors that exist in the cardiovascular, central nervous and immune systems. In targeting the S1P receptor, initiation of treatment with Gilenya is known to be associated with bradycardia (slowing of the heart rate) and atrioventricular (AV) block (a problem with electrical impulse conduction in the heart).

Gilenya is an effective prescription medicine proven to decrease the number of MS flare-ups (relapses) and slow down the physical problems MS causes. In a two-year study, Gilenya reduced annualized MS relapses by 54% (0.18 vs 0.40; P<0.001) and 52% (0.16 vs 0.33; P<0.001) at one year, when compared with placebo and interferon beta-1a IM, respectively. Additionally, Gilenya showed a 30% reduction in the risk of 3-month confirmed disability (p<0.05; key secondary endpoint) compared to placebo.

Indication

GILENYA is a prescription medicine used to treat relapsing forms of multiple sclerosis (MS) in adults.

GILENYA can decrease the number of MS flare-ups (relapses). GILENYA does not cure MS, but it can help slow down the physical problems that MS causes.

Important Safety Information

You should not take GILENYA if in the last 6 months you experienced heart attack, unstable angina, stroke or warning stroke, or certain types of heart failure. Do not take GILENYA if you have an irregular or abnormal heartbeat (arrhythmia) or if you take medicines that change your heart rhythm.

GILENYA may cause serious side effects such as:

• Slow heart rate, especially after your first dose. A test to check the electrical activity of your heart (ECG) will be performed before and six hours after your first dose. Your pulse and blood pressure should be checked every hour while you stay in a medical facility during this time. If your heart rate slows down too much, you might feel dizzy or tired, or feel like your heart is beating slowly or skipping beats. Symptoms can happen up to 24 hours after your first dose. After 6 hours, if your ECG shows any heart problems or if your heart rate is still too low or continues to decrease, you will continue to be watched by a health care professional. If you have any serious side effects after your first dose, especially those that require treatment with other drugs, you will stay in a medical facility to be watched overnight and for at least 6 hours after your second dose of GILENYA the next day. If you experience slow heart rate, it will usually return to normal within 1 month. Call your doctor or go to the nearest emergency room right away if you have any symptoms of a slow heart rate. If you stop taking GILENYA for more than 14 days, you will need to repeat this observation.

• Increased risk of serious infections. GILENYA lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within 2 months of stopping GILENYA. Your doctor may do a blood test before you start GILENYA. Increased risk of infection was seen with doses higher than the approved dose (0.5 mg). Two patients died who took higher-dose GILENYA (1.25 mg) combined with high-dose steroids. Call your doctor right away if you have fever, tiredness, body aches, chills, nausea, or vomiting.

• Macular edema, a vision problem that can cause some of the same vision symptoms as an MS attack (optic neuritis), or no symptoms. Macular edema usually starts in the first 3 to 4 months after starting GILENYA. Your doctor should test your vision before you start GILENYA; 3 to 4 months after you start GILENYA; and any time you notice vision changes. Vision problems may continue after macular edema has gone away. Your risk of macular edema may be higher if you have diabetes or have had an inflammation of your eye (uveitis). Call your doctor right away if you have blurriness, shadows, or a blind spot in the center of your vision; sensitivity to light; or unusually colored vision.

• Breathing problems. Some patients have shortness of breath. Call your doctor right away if you have trouble breathing.

• Liver problems. Your doctor should do blood tests to check your liver before you start GILENYA. Call your doctor right away if you have nausea, vomiting, stomach pain, loss of appetite, tiredness, dark urine, or if your skin or the whites of your eyes turn yellow.

• Increases in blood pressure (BP). BP should be monitored during treatment.

GILENYA may harm your unborn baby. Talk to your doctor if you are pregnant or planning to become pregnant. Women who can become pregnant should use effective birth control while on GILENYA, and for at least 2 months after stopping. If you become pregnant while taking GILENYA, or within 2 months after stopping, tell your doctor right away. Women who take GILENYA should not breast-feed, as it is not known if GILENYA passes into breast milk. A pregnancy registry is available for women who become pregnant during GILENYA treatment. Call 1-877-598-7237 for more information.

Tell your doctor about all your medical conditions, including if you had or now have an irregular or abnormal heartbeat; heart problems; a history of fainting; a fever or infection, or if you are unable to fight infections; eye problems; diabetes; breathing or liver problems; or high blood pressure. Also tell your doctor if you have had chicken pox or have received the vaccine for chicken pox. Your doctor may do a test for the chicken pox virus, and you may need to get the vaccine for chicken pox and wait 1 month before starting GILENYA.

Tell your doctor about all the medicines you take, including medicines for heart problems or high blood pressure or other medicines that may lower your heart rate or change your heart rhythm; medicines that could increase your chance of infections, such as medicines to treat cancer or control your immune system; or ketoconazole (an antifungal) by mouth. If taken with GILENYA, serious side effects may occur. You should not get certain vaccines while taking GILENYA, and for at least 2 months after stopping.

The most common side effects with GILENYA were headache, flu, diarrhea, back pain, abnormal liver tests, and cough.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

For full Prescribing Information and the Medication Guide log onto www.pharma.us.novartis.com.

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 Pharmaceuticals Corporation researches, develops, manufactures and markets innovative prescription drugs used to treat a number of diseases and conditions, including cardiovascular, dermatological, central nervous system, bone disease, cancer, organ transplantation, psychiatry, infectious disease and

respiratory. The company's mission is to improve people's lives by pioneering novel healthcare solutions.

Located in East Hanover, NJ, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which 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.

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8. Data on file.

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