New analysis shows Novartis drug Gilenya® significantly reduced rate of brain volume loss across three large Phase III studies

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- -- Data show reductions in rate of brain volume loss by about one-third compared to interferon beta-1a IM or placebo in studies with over 3,600 patients with relapsing MS1
- -- Gilenya is the first oral disease modifying treatment to show consistent effect on brain volume loss, an important indicator of disease progression
- -- Analysis of FREEDOMS II, a Phase III study, confirms Gilenya consistently reduces annualized relapse rates across disease activity, gender, age and prior treatment2
- -- Safety profile of Gilenya reinforced in patients treated up to four years3; more than 56,000 patients treated with Gilenya worldwide

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EAST HANOVER, N.J., March 21, 2013 /PRNewswire/ -- New data presented at the 65th annual meeting of the American Academy of Neurology (AAN) show Gilenya® (fingolimod), the first oral disease modifying therapy approved to treat relapsing forms of multiple sclerosis (MS), significantly and consistently reduced the rate of brain volume loss. Results also showed that Gilenya reduced annualized relapse rates across important subgroups; and additional data reinforce Gilenya's safety profile in patients treated up to four years.

"Loss of brain volume is a consequence of multiple sclerosis and is a key MRI correlate of disease progression," said Dr. Timothy Wright, Global Head Development, Novartis Pharmaceuticals AG. "The findings reported show the effect of Gilenya across a variety of important disease measures and support evidence for initiating early use of this highly effective treatment in patients with relapsing MS."

Data shows consistent reduction in rate of brain volume loss
In a new analysis of over 3,600 patients from three large Phase III studies (TRANSFORMS, FREEDOMS, and FREEDOMS II) Gilenya showed a significant reduction in the rate of brain volume loss vs. a comparator – consistent with previously reported results.[1] In the TRANSFORMS study over one year, Gilenya reduced the rate of brain volume loss by 32 percent ($p<0.001$) compared to Avonex® (interferon beta-1a IM), a commonly prescribed injectable treatment.[1] Over two years, Gilenya reduced the rate of brain volume loss compared to placebo by 35 percent ($p<0.001$) in the FREEDOMS study, and by 33 percent ($p<0.001$) in the FREEDOMS II study, respectively.[1]

The data also showed that brain volume, at baseline, consistently correlated with the level of disease severity and disability.[1] Lower brain volume was linked with more severe disease and disability, while higher brain volume correlated with less severe levels. In addition, traditional markers of disease activity (such as MRI lesion counts) at baseline were predictive of the rate of brain volume loss over two years.[1]

New results highlight consistent efficacy and long-term safety profile

Separately, a recent subgroup analysis (n=1083) of FREEDOMS II, the third large Phase III Gilenya study, supports the known efficacy of Gilenya treatment. Specifically, results show Gilenya consistently reduced annualized relapse rates (ARR) compared to placebo in patients with relapsing-remitting MS, across gender, age, prior treatment, and baseline disease activity.[2]

New extension data from FREEDOMS II (n=632) reinforce the known safety profile of Gilenya in patients treated up to four years.[3] More than eight out of ten patients (83 percent) completed the extension study, which identified no unexpected safety concerns.[3]

Gilenya was approved based on the largest Phase III program in relapsing-remitting MS at the time of submission. With up to seven years of clinical trial experience (Phase II and III) and over two years of real-world use, there is increasing experience of Gilenya's long-term effectiveness and safety profile in more than 56,000 patients treated worldwide; this includes clinical trial use and patients prescribed Gilenya.[4]

About Gilenya

Gilenya is the first oral disease modifying therapy (DMT) approved to treat relapsing forms of MS and the first in a class of compounds called sphingosine 1-phosphate receptor (S1PR) modulators. Gilenya is thought to act on inflammatory processes implicated in the MS disease process although the exact mechanism in MS is unknown.[5,6] 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).[6]

Gilenya is the only oral DMT for relapsing forms of MS with proven and consistent efficacy across two pivotal trials, including a head-to-head study (interferon beta-1a IM).[7,8] In a two-year study, Gilenya reduced annualized relapses by 54 percent ($p<0.001$) when compared to placebo.[8] In addition, Gilenya showed a 30 percent reduction in the risk of 3-month confirmed disability progression ($p=0.02$, key secondary endpoint) compared to placebo.[8] However, in a separate one-year study, there was no significant risk reduction of disability progression between Gilenya and Interferon beta-1a IM. Gilenya reduced annualized relapse rate by 52 percent ($p<0.001$) compared to interferon beta-1a IM in a one-year study. A two-year pivotal clinical trial has shown that the majority of patients who start on Gilenya stay on therapy compared to placebo (81.2 percent vs. 72.5 percent).[8] Gilenya is licensed from Mitsubishi Tanabe Pharma Corporation.

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 breastfeed, 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 or visit www.gilenyapregnancyregistry.com for more information.

Tell your doctor about all your medical conditions, including if you had or now have an irregular or abnormal heartbeat; history of stroke or warning stroke; 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.

Please see full Prescribing Information for Gilenya:
http://www.pharma.us.novartis.com/cs/www.pharma.us.novartis.com/product/pi/pdf/gilenya.pdf

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The foregoing release contains forward-looking statements that can be identified by express or implied discussions regarding potential new indications or labeling for Gilenya or regarding potential future revenues from Gilenya. 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 with Gilenya 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 submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that Gilenya will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Gilenya could be affected by, among other things, unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; 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.

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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, New Jersey, 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 2012, the Group achieved net sales of USD 56.7 billion, while R&D throughout the Group amounted to approximately USD 9.3 billion (USD 9.1 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 128,000 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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2. Goodin D. et al. Fingolimod reduces annualized relapse rates in patients with relapsing-remitting multiple sclerosis: FREEDOMS II study subgroup analysis. Abstract Presented at AAN, San Diego, March 2013.
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Novartis Media Relations

Julie Masow	Heather Swedin
Novartis Media Relations	Novartis US Pharma Communications
+1 212 830 2465 (direct)	+1 862 778 1414 (direct)
+1 862 579 8456 (mobile)	+1 917 859 4086 (mobile)
julie.masow@novartis.com	heather.swedin@novartis.com

e-mail: media.relations@novartis.com
For Novartis multimedia content, please visit www.thenewsmarket.com/Novartis
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significantly-reduced-rate-brain-volume-loss-across-three-large-phase-iii-studies
2. http://www.gilenyapregnancyregistry.com
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