

**MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG****Novartis oral MS therapy FTY720 shows reduced risk of confirmed disability progression as published in *New England Journal of Medicine***

- *Combined data from TRANSFORMS and FREEDOMS studies show significant efficacy in reducing relapses, disability progression and MRI lesions in MS*
- *In FREEDOMS, FTY720 0.5 mg dose reduced the risk of 3-month and 6-month confirmed disability progression by 30% and 37% over two years versus placebo*
- *FTY720 clinical program provides safety experience in over 2,300 MS patients, including some patients in their sixth year of therapy*
- *Robust clinical trial program strengthens potential for oral FTY720 to be the first approved product in new therapeutic class called S1P receptor modulators*
- *FTY720 0.5 mg dose submitted for regulatory approval in US and EU in December 2009*

**Basel, January 20, 2010** – Results of the TRANSFORMS<sup>1</sup> and FREEDOMS<sup>2</sup> studies, the two pivotal Phase III clinical trials with oral FTY720 (fingolimod), have been published in *The New England Journal of Medicine*, providing comprehensive evidence to support the efficacy and safety profile of this first-in-class therapy for multiple sclerosis (MS).

The data, from one of the largest Phase III programs conducted in MS, were included in the applications for regulatory approval submitted to the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) in December 2009. In both studies, two doses of FTY720 were examined (0.5 mg and 1.25 mg). Approval is sought for the lower 0.5 mg dose as the results from the studies indicate that this dose has the most positive benefit-risk profile.

“Innovative science leading to new medicines for MS patients is greatly needed,” said John Richert, MD, Executive Vice President for Research and Clinical Programs at the US National Multiple Sclerosis Society. “The positive results published in *The New England Journal of Medicine* showing benefit of fingolimod on the clinical and MRI outcomes assessed is very encouraging for MS patients, their families and their physicians.”

The one-year TRANSFORMS study involving 1,292 patients showed that oral FTY720 0.5 mg reduced relapses by 52% compared to interferon beta-1a (Avonex<sup>®</sup>)<sup>†</sup> given by intramuscular injection, while the reduction with FTY720 1.25 mg was 38% (both  $p < 0.001$ ). The two-year FREEDOMS study, involving 1,272 patients, showed that FTY720 reduced the relapse rate by 54% for the 0.5 mg dose and 60% for the 1.25 mg dose compared to placebo (both  $p < 0.001$ ). Patients on FTY720 0.5 mg also had a 30% lower risk of disability progression, three-month confirmed ( $p = 0.02$ ) and a 37% lower risk of disability progression, six-month confirmed ( $p = 0.01$ ) over two years compared to

placebo. Similarly, the FTY720 1.25 mg dose reduced the risk of three-month and six-month confirmed disability progression by 32% ( $p=0.02$ ) and 40% ( $p=0.006$ ) respectively.

In both studies, treatment with FTY720 also resulted in statistically significant reductions in brain lesion activity and reduced loss of brain volume as measured by magnetic resonance imaging (MRI).

“The TRANSFORMS data demonstrate the efficacy of fingolimod compared to a current standard of care. These findings may represent a real step forward in the fight against MS,” said Jeffrey Cohen, MD, TRANSFORMS study lead investigator and staff physician at the Cleveland Clinic Mellen Center for Multiple Sclerosis Treatment and Research in Cleveland, Ohio, USA. “Current disease-modifying therapies for relapsing-remitting MS are administered by injection or infusion, which may negatively affect tolerability, convenience, and compliance for patients on these therapies.”

Professor Ludwig Kappos, MD, principal investigator for the FREEDOMS clinical trial and Chair of Neurology and Research Group Leader in the Department of Biomedicine at the University Hospital in Basel, Switzerland, said: “FTY720 demonstrated clear clinical superiority over placebo in terms of reducing relapse rates and disability progression. The positive findings of TRANSFORMS and FREEDOMS give an increasingly complete understanding of the efficacy and safety of FTY720.”

Up to 2.5 million people worldwide are affected by MS, an inflammatory and neurodegenerative condition that often begins when patients are in the prime of their lives<sup>3</sup>.

FTY720 has the potential to be the first approved therapy in a new class of drugs called sphingosine 1-phosphate (S1P) receptor modulators. These medicines reduce inflammation and may also have a direct beneficial effect on cells in the central nervous system (CNS). FTY720 acts selectively by retaining certain lymphocytes (a sub-group of white blood cells) in the lymph nodes, reducing the number of lymphocytes that reach the brain where they can cause inflammatory destruction. This lymphocyte retention is reversible, allowing circulating lymphocytes to regain normal levels if treatment is stopped.

“These data demonstrate that oral FTY720 has the potential to offer an important new treatment option for patients with MS,” said Trevor Mundel, MD, Global Head of Development at Novartis Pharma AG. “We have a long-term commitment to the MS community, and trust that FTY720, once approved, will prove to be a valuable treatment option for many people who live with this disease.”

In both TRANSFORMS and FREEDOMS, adherence to therapy was best for the FTY720 0.5 mg and control groups compared to the 1.25 mg group. The most commonly reported adverse events for both FTY720 and control groups were nasopharyngitis, headache and fatigue. FTY720-related adverse events included dose-related, transient, generally asymptomatic heart rate reduction, infrequent transient AV conduction block, mild (1-3 mm Hg) blood pressure increase, macular edema (more common with 1.25 mg than the 0.5 mg target dose), and asymptomatic, reversible elevation of liver enzymes.

The rates of infections overall, including serious infections, were comparable between treatment groups, although a slight increase in lung infections (primarily bronchitis) was seen in patients treated with FTY720. The number of malignancies reported in the two studies was small with comparable rates between the FTY720 and control groups; malignancies were reported more frequently with FTY720 than the control group in the one-year TRANSFORMS study but the opposite pattern was seen in the two-year FREEDOMS study.

Serious adverse events were comparable between treatment groups, though generally slightly higher with the 1.25 mg than 0.5 mg dose. Overall rates of drug-related adverse events, particularly those related to the mechanism of action, as well as discontinuations due to adverse events, were more common with 1.25 mg than 0.5 mg.

The completed MS FTY720 studies and their extensions include more than 2,300 patients with approximately 4,000 patient-years of exposure, including some patients now in their sixth year of treatment. Safety is also being monitored in approximately 1,000 additional patients in ongoing MS studies.

The publication in *The New England Journal of Medicine* marks the first presentation of full results from the two studies. Top line results of FREEDOMS and TRANSFORMS have been disclosed in Novartis press releases, and the TRANSFORMS study has also been presented at scientific congresses<sup>4</sup>.

†Avonex<sup>®</sup> is a registered trademark of Biogen Idec.

Dr. Jeffrey Cohen conducts research and is a paid consultant for Novartis.

### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as "risk," "potential," "encouraging," "may," "can," "commitment," "will," or similar expressions, or by express or implied discussions regarding marketing approvals for FTY720 or regarding potential future revenues from FTY720. 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 FTY720 to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that FTY720 will be approved for sale in any market. Nor can there be any guarantee that FTY720 will achieve any particular levels of revenue in the future. In particular, management's expectations regarding FTY720 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; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry and general public pricing pressures; 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 healthcare solutions that address the evolving needs of patients and societies. Focused solely on healthcare, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic pharmaceuticals, preventive vaccines, diagnostic tools and consumer health products. Novartis is the only company with leading positions in each of these areas. In 2008, the Group's continuing operations achieved net sales of USD 41.5 billion and net income of USD 8.2 billion. Approximately USD 7.2 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 99,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit <http://www.novartis.com>.

## References

- 1 Cohen J. et al. Oral Fingolimod vs. Intramuscular Interferon in Relapsing Multiple Sclerosis. N Eng J Med. Vol.362 No.5, Feb 4, 2010 (printed version).
- 2 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 (printed version).
- 3 National Multiple Sclerosis Society website. <http://www.nationalmssociety.org/about-multiple-sclerosis/what-is-ms/index.aspx>. Last accessed Jan 15, 2010.
- 4 Cohen J. et al. Oral Fingolimod (FTY720) Versus Interferon Beta-1a in Relapsing-Remitting Multiple Sclerosis: Results from a Phase III Study (TRANSFORMS). Slide deck associated with Oral Presentation at the American Academy of Neurology Annual Meeting 2009. [S21.004].

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## Novartis Media Relations

**Central media line :** +41 61 324 2200

### Eric Althoff

Novartis Global Media Relations  
+41 61 324 7999 (direct)  
+41 79 593 4202 (mobile)  
eric.althoff@novartis.com

### Åsa Josefsson

Novartis Pharma Communications  
+41 61 324 0161 (direct)  
+41 79 515 2253 (mobile)  
asa.josefsson@novartis.com

e-mail: [media.relations@novartis.com](mailto:media.relations@novartis.com)

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## Novartis Investor Relations

**Central phone:** +41 61 324 7944

Ruth Metzler-Arnold +41 61 324 9980  
Pierre-Michel Bringer +41 61 324 1065  
John Gilardi +41 61 324 3018  
Thomas Hungerbuehler +41 61 324 8425  
Isabella Zinck +41 61 324 7188

### North America:

Richard Jarvis +1 212 830 2433  
Jill Pozarek +1 212 830 2445  
Edwin Valeriano +1 212 830 2456

e-mail: [investor.relations@novartis.com](mailto:investor.relations@novartis.com)

e-mail: [investor.relations@novartis.com](mailto:investor.relations@novartis.com)