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First Phase III results for FTY720, a novel oral therapy for MS, show superior efficacy compared to interferon beta-1a

- *FTY720 significantly reduced annualized relapse rates by 52% (0.5 mg dose) and 38% (1.25 mg) vs. interferon beta-1a in one-year TRANSFORMS study¹*
- *FTY720 generally well-tolerated and safety profile in line with previous experience¹*
- *Regulatory submissions for FTY720 in US and EU on track for end of 2009; FREEDOMS and FREEDOMS II placebo-controlled Phase III studies continuing*
- *Multiple sclerosis, a devastating disease causing progressive disability, affects up to 2.5 million people worldwide including many young adults²*

Basel, December 12, 2008 — Initial results from the one-year Phase III TRANSFORMS study show the investigational oral compound FTY720 (fingolimod) has superior efficacy to a current standard of care for patients with relapsing-remitting multiple sclerosis (MS). Patients on oral FTY720 experienced significantly fewer relapses than those treated with the injectable medicine interferon beta-1a (Avonex^{®*})¹.

The study, the first one-year head-to-head Phase III trial against a standard of care in MS, met its primary endpoint for both doses of FTY720.

The annualized relapse rate at one year for patients given FTY720 0.5 mg was 0.16, representing a 52% reduction compared to a relapse rate of 0.33 for interferon beta-1a ($p < 0.001$). The FTY720 1.25 mg dose also showed a significant reduction in relapses with a rate of 0.20 representing a 38% reduction against interferon beta-1a ($p < 0.001$). No statistically significant difference was seen between the two FTY720 doses¹.

Comprehensive analyses of the TRANSFORMS study data are ongoing, and detailed results are planned to be presented at a leading scientific congress in 2009. Regulatory submissions remain on track to be completed in the US and EU at the end of 2009.

“We are encouraged by the early results from TRANSFORMS, which represent a major step towards delivering an effective oral treatment for people with relapsing-remitting MS,” said Trevor Mundel, MD, Global Head of Development at Novartis Pharma AG. “These positive results reinforce the potential for FTY720 to provide a significant advance in the future treatment of this devastating disease.”

MS is a chronic autoimmune neurodegenerative disease of the central nervous system associated with irreversible progression of disability³. As many as 2.5 million people worldwide are affected by the condition² that typically begins in early adulthood between the ages of 20 and 40 years when patients are in the prime of life⁴.

TRANSFORMS (TRial Assessing injectable interferoN vS FTY720 Oral in RrMS) is the first of three studies to report results in one of the largest Phase III clinical programs ever conducted in MS, involving more than 3,400 patients around the world.

As a head-to-head trial against interferon beta-1a, TRANSFORMS was designed to assess the efficacy of FTY720 compared to an established disease-modifying therapy in reducing relapse rates in patients with relapsing-remitting MS, the most common form of the disease. Two other studies – FREEDOMS and FREEDOMS II – are two-year placebo-controlled Phase III studies to assess the impact of FTY720 in reducing the frequency of relapses and slowing the progression of disability, and to further characterize the benefit-risk profile. Data from these studies to support regulatory submissions are expected in 2009.

TRANSFORMS was a one-year worldwide double-blind, double-dummy study that enrolled 1,292 patients. The study had three arms: oral FTY720 0.5 mg and 1.25 mg once-daily, and the active comparator interferon beta-1a given once-weekly by intra-muscular injection. The patient population in TRANSFORMS was consistent with the demographics and disease state seen in Phase III clinical trials for other disease-modifying treatments for relapsing-remitting MS⁵.

The safety profile of FTY720 seen in TRANSFORMS was in line with previous clinical experience. The compound was generally well-tolerated with 87% of FTY720-treated patients completing the study on treatment. The proportion of patients discontinuing therapy was 10% in the FTY720 0.5 mg group, 15% in the FTY720 1.25 mg group, and 12% in the interferon beta-1a group¹.

The most commonly reported adverse events, seen in more than 10% of patients in all three study arms, were headache, nasopharyngitis and fatigue. Influenza-like symptoms were reported in 37% of patients treated with interferon beta-1a and in 4% of patients treated with FTY720¹.

Adverse effects seen in FTY720-treated patients included transient reductions in heart rate at the start of treatment, minor increases in blood pressure, and elevations in liver enzymes (also seen with interferon beta-1a). Macular edema (swelling of the center of the retina) was detected in less than 1% of FTY720-treated patients¹. Seven cases of localized skin cancer were diagnosed in FTY720-treated patients (four basal cell carcinoma and three melanoma), while one case of squamous cell carcinoma was seen in the interferon beta-1a group. All of these localized skin lesions were successfully removed¹.

As previously reported, two fatal herpes infections occurred in patients treated with FTY720 1.25 mg. Both cases involved confounding factors impacting the outcome, but a role for FTY720 could not be excluded given its immunosuppressive effect.

In general, the safety profile of the FTY720 0.5 mg dose appeared to be better than that of the 1.25 mg dose, including lower rates of infections and bradycardia. Further analyses of the TRANSFORMS data and results from the ongoing Phase III studies will help to provide a more comprehensive assessment of FTY720's benefit-risk profile.

* Avonex® is a registered trademark of Biogen Idec.

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The foregoing release contains forward-looking statements that can be identified by terminology such as “on track,” “planned,” “encouraged,” “potential,” “to assess,” “to further characterize,” “expected,” “appeared to be,” “will,” or similar expressions, or by express or implied discussions regarding potential regulatory submissions or 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 submitted for approval in any market by the end of 2009 or at any time. Nor can there be any guarantee that FTY720 will ever be approved for sale in any market. Neither 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 clinical trial results, including unexpected new clinical data (including the upcoming results of the FREEDOMS and FREEDOMS II trials) and unexpected additional analysis of existing clinical data (including the results of the ongoing additional analyses of the TRANSFORMS clinical data); unexpected regulatory actions or delays or government regulation generally; competition in general; the company’s ability to obtain or maintain patent or other proprietary intellectual property protection; 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.

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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

John Taylor

Novartis Pharma Communications

+41 61 324 6715 (direct)

+41 79 593 4279 (mobile)

john.taylor@novartis.com

e-mail: media.relations@novartis.com

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

e-mail: investor.relations@novartis.com