

NOVARTIS AG  
Form 6-K  
November 02, 2005

## **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 for October 2005**

**(Commission File No. 1-15024)**

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**Novartis AG**

**(Name of Registrant)**

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Yes:  No:

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Enclosures:

1. Xolair® granted marketing authorization in Europe as novel therapy for severe allergic asthma (Basel, October 27, 2005)
2. Study shows conversion to Myfortic® from current therapy significantly improved quality of life for kidney transplant patients (Geneva, October 19, 2005)
3. World experts convene in Tanzania to address tuberculosis (TB) emergency (Bagamoyo, Tanzania, October 17, 2005)
4. New research shows benefits of Elidel® in eczema patients who require an alternative to conventional steroid treatment (Basel, October 14, 2005)
5. FTY720 Phase II 12-month data show sustained benefits and good tolerability in patients with relapsing multiple sclerosis (Basel, October 1, 2005)

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**- Investor Relations Release -**

**Xolair® granted marketing authorization in Europe as novel therapy for severe allergic asthma**

*Xolair provides asthma patients with one of the most significant advances in last 15 years*

*The first monoclonal antibody approved for the treatment of asthma in Europe*

**Basel, October 27, 2005** Novartis announced today that the European Commission has granted Marketing Authorization in all 25 EU member states for the novel asthma therapy Xolair® (omalizumab), considered by many experts to be one of the most significant advances in the last 15 years for helping patients with asthma.

Xolair's unique mechanism of action addresses the need to provide patients with a new injectable treatment that effectively controls asthma attacks and symptoms that often remain uncontrolled with current therapies.

As the first monoclonal antibody to be approved for the treatment of asthma, Xolair offers a unique therapeutic approach by blocking the action of IgE, an underlying cause of symptoms in allergic disease. Xolair is expected to become available in the first European countries within the next few weeks.

Xolair represents a real advance in the management of asthma, having shown long-term efficacy and safety, said Professor Stephen Holgate of Southampton General Hospital, UK. This approval provides a much-needed breakthrough in the fight against severe allergic asthma. It's exciting to know that we finally have a treatment approach that has the potential to transform the lives of those who have been previously debilitated by this condition and for whom previously we have had little to offer.

Patients with severe asthma are at greatest risk of hospitalization and death.(1),(2) According to the World Health Organization, more than 12,000 deaths are linked to asthma in Western Europe every year.(3) Asthma affects an estimated 30 million people in Europe, with up to 90% experiencing allergic asthma and attacks often being triggered by

environmental factors such as pollen, animal dander and dust mites.(4),(5) Around 20% of people with asthma in Western Europe are classified as having severe disease,(6) and within this group some continue to experience inadequately controlled symptoms despite taking the best available therapy.(7)

We believe Xolair is one of the most significant advances in asthma treatment in the last 15 years and are pleased that patients in Europe will now be able to benefit from this highly innovative

therapy, said Joerg Reinhardt, Global Head of Development Novartis Pharma AG. Novartis is proud to bring a medicine to the European markets that offers the potential for effective control of asthma attacks and symptoms in even patients with the most severe disease, where patients have been at significant risk of asthma exacerbations, hospitalization and death.

#### More about Xolair

Xolair is administered by injection under the skin every two or four weeks, and targets the IgE antibody which is a root cause of the inflammatory cascade of symptoms in diseases such as allergic asthma. Clinical studies have shown that it significantly reduced the rate of asthma exacerbations (or attacks) and halved the rate of emergency medical visits in patients with severe persistent asthma.(8) Benefits were seen even in patients whose asthma was inadequately controlled despite using the best available therapy(8) and who were, as a consequence, at increased risk of life-threatening attacks.(1),(2)

In Europe, Xolair is licensed as add-on therapy to improve asthma control in adults and adolescents (aged 12 and above) with severe persistent allergic asthma, who have the following, despite daily high-dose inhaled corticosteroids plus a long-acting inhaled beta2-agonist:

a positive skin test or *in vitro* reactivity to a perennial aeroallergen

reduced lung function (FEV1 <80%)

frequent daytime symptoms or night-time awakenings

multiple documented severe asthma exacerbations

Xolair treatment should only be considered for patients with convincing IgE-mediated asthma.

Xolair was approved by the US Food and Drug Administration (FDA) in June 2003. It has been prescribed to more than 52,000 patients worldwide following its approval, which includes other countries such as Australia, Brazil, Canada and Venezuela. Xolair has been developed under an agreement between Novartis Pharma AG, Genentech and Tanox.

The use of Xolair is supported by a comprehensive program of more than 30 clinical trials involving a total of approximately 5,500 patients. These demonstrated Xolair's efficacy in controlling symptoms, reducing asthma exacerbations and the need for emergency medical treatment, and improving quality of life, even in patients with severe allergic asthma that was uncontrolled by existing medication. Recent long-term data have shown that effective control was maintained for more than three years with Xolair, and that patients experienced improvements in their lung function and reductions in the need for inhaled corticosteroids.(9)

The potential benefits of anti-IgE therapy are already recognized in treatment guidelines such as those developed by the Global Initiative for Asthma (GINA). These recommend anti-IgE therapy as add-on treatment for patients with severe allergic asthma that is inadequately controlled by standard clinical options.(10)

The foregoing release contains certain forward-looking statements that can be identified by terminology such as will , is expected to , potential , long-term , or similar expressions, or by express or implied discussions regarding the potential that Xolair will be approved for sale in any additional markets, or regarding any potential future revenues from Xolair. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Xolair to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Xolair will be approved

for sale in any additional market, or that it will achieve any particular sales level. In particular, management's expectations regarding commercialization of Xolair could be affected by, among other things, uncertainties relating to clinical trials; new clinical data, or additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; 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; as well as other risks and factors referred to in the Company'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 AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2004, the Group's businesses achieved net sales of USD 28.2 billion and pro forma net income of USD 5.6 billion. The Group invested approximately USD 4.1 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 91,700 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

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**MEDIA RELEASE      COMMUNIQUE AUX MEDIAS      MEDIENMITTEILUNG**

**Study shows conversion to Myfortic® from current therapy significantly improved quality of life for kidney transplant patients**

*First-ever study in transplant patients utilized patient-reported measurement tools to differentiate between quality of life of existing therapies*

**Geneva, October 19, 2005** Results of the PROGIS study released at the European Society for Organ Transplant (ESOT) meeting showed that 66% of patients who suffered gastrointestinal (GI) complaints while on mycophenolate mofetil (MMF) following kidney transplantation surgery reported an overall improvement in GI symptoms when converted to Myfortic® (enteric coated mycophenolate sodium).

Data from PROGIS (Patient Reported Outcomes in renal transplant patients with or without Gastro-Intestinal Symptoms) also showed that converting MMF patients who experienced GI problems to Myfortic significantly reduced their symptom burden while significantly improving their gastrointestinal and general well-being ( $p < 0.001$ ).

These findings provide for the first time in transplantation insight into the value of patient-reported measurement tools as a way of differentiating the impact of adverse events with immunosuppressive therapies. This study also confirmed that MMF-associated gastro-intestinal effects had a significant impact on the health-related quality of life and psychological well-being of the study patients.

Patient Reported Quality of Life measurements have been used successfully in other treatment areas such as oncology, said Professor Paul Keown, MD, Director of Immunology and Head of Nephrology at the University of British Columbia. This is the right time to apply these assessment tools to transplant patients to further our understanding of how to improve care in patients who have gone through very intensive medical management.

Dr Shamkant Mulgoankar, Chief of the Division of Transplantation for the St Barnabas Health Care System and one of the leading investigators in the study, said: These first data are very encouraging results for the transplant community as this is the first study to evaluate patient functioning and well-being among patients converted from MMF to Myfortic because of GI complaints. Clinicians can now use these results to guide their considerations of treatment options for patients with GI complaints.

PROGIS is an open-label, multicenter, longitudinal study that utilised four different patient-reported Quality of Life questionnaires to identify the burden of gastrointestinal symptoms related to the two mycophenolic acid formulations (Myfortic and MMF) in kidney transplanted patients.

Changes in GI-specific symptoms burden from baseline were reported by patients using the Gastrointestinal Symptoms Rating Scale (GSRS) as well as the Overall Treatment Effect (OTE) scale after four to six weeks of treatment. Other scales used were GIQLI (GI Quality of Life Index) and PGWBI (Psychological Well-Being Index).

Myfortic is an enteric-coated formulation of mycophenolic acid and is approved in over 50 countries, including the US and major European countries. Myfortic is indicated for the prophylaxis of acute transplant rejection in patients receiving allogeneic renal transplants in combination with ciclosporin for microemulsion and corticosteroids.

This release contains certain forward-looking statements that can be identified by the use of forward-looking terminology, such as "are very encouraging", or similar expressions, or by express or implied discussions regarding the potential benefits and the potential future sales of Myfortic. Such forward-looking statements reflect the current views of the Company regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause the actual results with Myfortic to be materially different from any future results, performance, or achievements expressed or implied by such statements. There can be no guarantee that Myfortic will reach any particular sales levels. Any such results can be affected by, among other things, uncertainties relating to clinical trials, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection, competition in general, government, industry, and general public pricing pressures, as well as factors discussed in the Company's Form 20-F filed 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 described herein as 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**

The Novartis Transplantation and Immunology Business Unit is committed to developing an innovative range of therapeutic products for the prevention of organ rejection, in order to provide an extensive choice of drugs to the transplant community and to maintain the role of Novartis as a global market leader in this field of medicine.

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**MEDIA RELEASE      COMMUNIQUE AUX MEDIAS      MEDIENMITTEILUNG**

**World experts convene in Tanzania to address tuberculosis (TB) emergency**

***TB kills half a million patients a year in Africa alone, two million globally***

***Resistant strains demand improved therapies and compliance***

***Health professionals, experts and patients unite to further efforts to reach Millennium Goals of halving TB prevalence and death***

**Bagamoyo, Tanzania, October 17, 2005** International experts at a symposium sponsored by the Novartis Institute for Tropical Diseases (NITD) are meeting to review advances in research on tuberculosis (TB) therapies. The meeting is addressing goals and problems of TB control with focus on Africa as well as latest trends in TB drug discovery and development.

The four-day symposium, which began on Monday, has brought together more than 120 scientific, medical and public health experts to assess current approaches to controlling TB and to discuss new ways of finding effective medicines to treat millions of patients worldwide.

Despite advances in therapies, TB still remains the most common infectious disease in the world and an urgent public health issue, said Prof. Paul Herrling, Head of Corporate Research at Novartis and Chairman of the Board of NITD. We must intensify our joint efforts to find new treatment options for millions of TB patients, particularly offering hope for those with multi-drug-resistant strains. One of the main strategic objectives is to shorten the duration of TB treatment and overcome persistence.

In the face of half a million deaths every year, WHO has declared a TB emergency in Africa. There is an urgent need to develop better tools for treatment and prevention of the disease in order to achieve the Millennium Development Goal of halving TB prevalence and deaths by 2015.

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The timing and location of the NITD Symposium demonstrates the commitment of the R&D community to contribute to this effort. said Prof. Douglas Young, Medical Microbiology, Imperial College London.

The presentation at the opening session on October 17 was made by the Honorable Anna Abdallah, the health minister of Tanzania. Other speakers included Dr. Ted Bianco, director of technology transfer at the Wellcome Trust, and Prof. Valerie Mizrahi at University of the Witwatersrand, South Africa.

Workshops on the remaining days of the symposium will highlight the goals and problems

inherent in TB control, particularly the emergence of multi-drug-resistant TB strains, and will also review the history and future of TB drug discovery and development. Many public-private partnerships are represented at the symposium, including the Bill and Melinda Gates Foundation, the Global Alliance for TB Drug Development and the Wellcome Trust.

#### **About Tuberculosis (TB)**

TB is a highly contagious disease caused by the bacterium *Mycobacterium tuberculosis*. Like the common cold, it is a contagious disease spread through the air by coughing and sneezing. TB is a curable disease, with isoniazid and rifampicin the two most powerful anti-TB drugs. However, the duration of treatment is several months resulting in compliance issues leading to resistant strains.

As the most common major infectious disease today, TB infects two billion people or more than one-third of the world's population and kills approximately two million people each year. The global epidemic is growing and becoming more dangerous. The neglect of TB control programs, HIV/AIDS and immigration have caused the disease to spread, and the emergence of multi-drug-resistant TB strains are contributing to the worsening impact of this disease. It is estimated that between 2002 and 2020, approximately one billion people will be newly infected, over 150 million people will get sick and 36 million will die of TB if controls are not improved. In Eastern Europe and Africa, TB deaths are increasing after almost 40 years of decline. In terms of numbers of cases, the biggest burden of TB is in Southeast Asia.

#### **Novartis commitment to the fight against TB**

Novartis is committed to helping patients with TB by sponsoring research programs at NITD as well as by donating drugs.

Researchers at NITD are applying new genomics and bioinformatics technologies to develop novel treatments for multi-drug resistant TB. NITD researchers plan to take advantage of the genome sequence of *Mycobacterium tuberculosis*, which has been available for more than five years. The challenge is to use this newly gained knowledge to identify novel targets which can be used for discovering new drug candidates. Any resulting drugs will be available to poor patients without profit in those developing countries where the disease is endemic.

Separately, Novartis announced in December 2003 a five-year partnership with the World Health Organization (WHO) to donate drugs that will help more than 500,000 TB patients. Novartis is donating anti-TB drugs to the Global Drug Facility, which is hosted by the WHO and operated by the Stop TB Partnership. The facility has supplied procurement support and medicines to more than three million TB patients in 65 countries since its launch. The drugs will be provided over a five-year period to countries scaling up TB control with support from the Global Fund to fight HIV/AIDS, Tuberculosis and Malaria.

The directly observed therapy short-course (DOTS) strategy closely monitors the treatment of patients and the proper administration of drugs during the treatment period. It consists of five key elements, including government commitment to sustained TB control as well as regular and uninterrupted supply of high-quality anti-TB drugs. Since its introduction in 1991, more than 17 million patients have received treatments under the DOTS strategy.

#### **About the NITD**

The Novartis Institute for Tropical Diseases (NITD) is one of Novartis' contributions to help reduce the global disease burden, particularly infectious diseases, and solve the problem of access to medicines to poor patients.



The NITD is set up as a public-private partnership between Novartis and the Singapore Economic Development Board. Its current research projects are mainly focused on Dengue fever and Tuberculosis. The institute performs basic and conceptual research for identification of targets, develops screening assays, and works on synthesis and optimization of compounds up to readiness for clinical testing.

The NITD intends to become a leading center for knowledge and education by offering exceptional teaching and training opportunities for biomedical scientists around the world and by transferring Novartis drug discovery know-how to the developing world. Furthermore, the NITD promotes strong partnerships with other institutions and universities on a global scale to leverage its research efforts to bring novel attractive compounds to patients by 2012.

#### **About Novartis**

Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2004, the Group's businesses achieved sales of USD 28.2 billion and pro forma net income of USD 5.8 billion. The Group invested approximately USD 4.2 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 83,700 people and operate in over 140 countries around the world.

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**MEDIA RELEASE      COMMUNIQUE AUX MEDIAS      MEDIENMITTEILUNG**

**New research shows benefits of Elidel® in eczema patients who require an alternative to conventional steroid treatment**

*Over 46% of Elidel patients clear or almost clear of facial eczema after six weeks*

*Elidel may reverse effects of skin thinning resulting from conventional treatments*

**Basel, October 14, 2005** The importance of Elidel (pimecrolimus) Cream 1% as an alternative to topical corticosteroids has been demonstrated by the results of a new study in which Elidel cleared eczema from the faces of patients allergic to or intolerant of steroids.(1) The study found 46.5% of patients treated with Elidel after six weeks were clear or almost clear of facial eczema compared to 16.2% of the group treated with unmedicated placebo vehicle cream (p<0.001).

These findings are especially compelling since atopic eczema often occurs on sensitive skin and because disease flare-ups may recur over long periods of time. So, many patients require an alternative to topical steroids, said Dr. Neil Shear of Sunnybrook and Women's College Health Sciences Centre and University of Toronto Medical School, Canada, who presented the results today at the congress of the European Academy of Dermatology and Venereology. This study demonstrates that Elidel provides a safe and effective option that can be used intermittently to treat sensitive skin when steroids are inappropriate or to provide a break from frequent use of steroids.

Topical steroids have been the mainstay of therapy for up to half-a-century, but their long-term use has been associated with a range of harmful side effects. Of the 200 patients enrolled in the study, a total of 45.9% had previously experienced potentially irreversible consequences such as rosacea (redness), atrophy (skin thinning) or telangiectasias (spider veins). Some were allergic to steroids (21.5%) or had eczema in areas where steroid use is inadvisable, such as around the eyes (17.5%) or on the eyelids (10.5%).

A special concern was that 82.5% of participants were dependent on steroids to reduce the painful and distressing symptoms of atopic eczema and were using them so frequently that there was an unacceptable risk of side effects (i.e. for an average of 17 days [±7.7] within the previous month). Elidel, one of a class of drugs called topical calcineurin inhibitors, does not contain steroids and acts more selectively to reduce the

inflammatory symptoms of atopic eczema.(2)

### **Significant improvement with Elidel**

Patients age 12 and above with a history of mild or moderate atopic eczema were enrolled at 29 centers in five countries. They were randomised into two groups for treatment with either Elidel or vehicle cream during a six-week double-blind phase, followed by six weeks of open label therapy. Efficacy was assessed using standard measures of disease severity such as the Investigator's Global Assessment (IGA).

As early as eight days after starting treatment, patients treated with Elidel began to show a significantly greater improvement than those using vehicle cream, with 20.8% of those on Elidel being clear or almost clear of facial eczema compared to 7.1% of those on vehicle ( $p < 0.01$ ). When the double-blind phase ended on day 43, the difference between the groups was even more pronounced (46.5% vs. 16.2% being clear or almost clear). Elidel patients maintained their improvement during the open label phase.

Reduction of itching (pruritus), one of the most troubling symptoms of eczema, was significantly greater in Elidel patients, with 69.3% achieving a pruritus score at day 43 of  $\leq 1$  (where 1 is defined as mild), compared to 34.5% of those on vehicle ( $p < 0.001$ ).

In addition, the study showed that Elidel helped to reverse the effects of skin thinning (or atrophy). After six weeks, 46% of Elidel patients who had skin atrophy at the start of the study experienced an improvement ( $p < 0.01$ ), compared to 19% of patients treated with vehicle cream.

Elidel was well-tolerated, and safety results were consistent with other studies using the drug.

### **Benefits of early treatment**

Atopic eczema has traditionally been treated reactively, using topical steroids to manage periodic flare-ups in which the skin becomes abnormally dry, itchy and inflamed, and scratching leads to broken, oozing and bleeding skin. With the availability of calcineurin inhibitors such as Elidel, physicians have been able to progress from reactive treatment to earlier proactive intervention to control the disease.

Results from two associated clinical trials also presented at the EADV congress, called the Pimecrolimus in Eczema: Prevention of Progression (PEP) studies, demonstrate that early intervention with Elidel at the first signs or symptoms of disease reduced the number and severity of flare-ups in children and adults.<sup>(3),(4)</sup>

The two 26-week, multi-center, double-blind, vehicle-controlled studies involved 521 children and adolescents (age 2-17 years) and 543 adults (age 18 or above) respectively, with a history of mild to moderate atopic eczema. Flare-ups were defined as a worsening of symptoms despite study treatment, requiring the use of topical steroids.

In the paediatric study,<sup>(3)</sup> the mean number of flares-ups was halved in the Elidel group compared to the vehicle group (0.84 vs. 1.68 flare-ups), while the adult study<sup>(4)</sup> showed a 30% reduction (0.97 vs. 1.39). Elidel-treated patients remained flare-free for longer, with a median time to first flare of more than 190 days in both studies, compared to 59 days for children and 67 days for adults treated with vehicle cream (both  $p < 0.0001$ ).



Children treated with Elidel at the first signs and symptoms of disease were able to shorten their use of topical steroids by 41% compared to those using vehicle (mean duration of steroid use: 12.9 vs. 21.9 days), while adults achieved a 21% reduction (17.7 vs. 22.5 days). Furthermore, patients using Elidel made at least one-third fewer unscheduled visits to their physician than those using vehicle (87 vs. 246 visits for children, 156 vs. 223 for adults). Elidel was well-tolerated and safety results were consistent with other studies using the drug.

Dr Shear commented: These clinical data demonstrate that Elidel is most effective when used proactively to treat atopic eczema at the very first signs or symptoms of recurrence (e.g. itching and redness), so preventing the majority of patients progressing to a major flare. When used in this manner, early intermittent treatment with Elidel over the long-term provides atopic eczema control, and supports a paradigm shift towards treating the disease proactively with Elidel and reserving topical corticosteroids as rescue therapy for major flares.

### **About Elidel**

Elidel has been shown to be an effective treatment for the management of mild to moderate eczema, with a favorable safety profile. It is the only non-steroid prescription cream approved for the short-term and intermittent long-term treatment of mild to moderate eczema in patients as young as two years old, who do not respond well to, or may have side effects from, conventional treatments.

Novartis is in product labeling discussions with the FDA and a number of other health authorities, after an FDA Advisory Committee in February 2005 recommended the inclusion of a boxed warning for Elidel and Protopic® (Astellas) relating to a theoretical risk of lymphoma. Novartis and many independent medical experts do not agree that such an action would be justified. Novartis remains confident in the safety and efficacy of Elidel in its approved indications.

The foregoing release contains certain forward-looking statements that can be identified by terminology such as long-term, supports a paradigm shift, is in product labeling discussions, remains confident, or similar expressions, or by express or implied discussions regarding Novartis product labeling discussions with the FDA and other health authorities, or any potential revenues from Elidel. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Elidel to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee regarding the outcome of Novartis product labeling discussions with the FDA and other health authorities, or that Elidel will reach any particular sales levels. In particular, management's expectations regarding commercialization of Elidel could be affected by, among other things, uncertainties relating to clinical trials; new clinical data; additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally, including the outcome of Novartis product labeling discussions with the FDA and other health authorities; 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; as well as other risks and factors referred to in the Company'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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**- Investor Relations Release -**

**FTY720 Phase II 12-month data show sustained benefits and good tolerability in patients with relapsing multiple sclerosis**

**Basel, October 1, 2005** Data from the extension of a Phase II study to 12 months confirm the significant effects of FTY720, a novel oral medication, for the treatment of patients with relapsing multiple sclerosis (MS).

The data, presented at theECTRIMS/ACTRIMS 21st Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS)/10th Annual Meeting of the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) meeting in Thessalonica, Greece, showed that both patient groups taking FTY720 (1.25 mg and 5 mg) who had experienced a reduction in their annualized relapse rate. A relapse refers to the appearance of new symptoms or the aggravation of old ones, lasting for at least 24 hours. rate of more than 50% during the first six months of the study compared to placebo maintained this low relapse rate during the subsequent six-month extension.

In patients who switched from placebo to either the 1.25 mg or 5 mg dosing of FTY720 after six months, the annualized relapse rate was reduced by at least 70% during the second six-month study phase compared to the first six months on placebo.

More than 80% of patients who received FTY720 for up to 12 months were free from lesions showing active inflammation on magnetic resonance imaging (MRI) at month twelve irrespective of their FTY720 treatment dose (1.25 mg or 5 mg).

We are excited by these full-year study results confirming the significant effect of oral FTY720 on reducing both clinical relapses and inflammatory disease activity that we first saw during the six-month placebo-controlled phase of the study, said chief investigator Professor Ludwig Kappos, MD, Department of Neurology at the University Hospital in Basel, Switzerland. We hope that the magnitude of benefits shown in Phase II will be confirmed in the larger scale Phase III study program expected to be launched soon.

Based on the positive Phase II study results, Novartis is in discussions with regulatory authorities about the FTY720 Phase III program, which is expected to be launched by the end of 2005.

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Over two million people worldwide are estimated to suffer from multiple sclerosis, which is the leading cause of neurological disability in young adults. Multiple Sclerosis International Federation ([http://www.msif.org/en/ms\\_the\\_disease/quick\\_facts.html](http://www.msif.org/en/ms_the_disease/quick_facts.html)) MS is the most common chronic, disabling disease of the central nervous system affecting twice as many women than men.<sup>3</sup> MS has a significant impact on the patient's social activities, employment and overall quality of life. Currently marketed MS therapies afford an average reduction in relapse rates of 30% in two-year

studies and require frequent injections ranging from daily to weekly. PRISMS study group. Randomised double-blind placebo-controlled study of interferon beta-1a in relapsing-remitting multiple sclerosis. *The Lancet* 1998; Vol 352: 1498-1504., LD Jacobs et al. Intramuscular Interferon beta-1a for disease progression in relapsing multiple sclerosis. *Ann Neurol* 1996, 39: 285-294., IFNB Multiple Sclerosis Study Group. Interferon beta-1b is effective in relapsing-remitting multiple sclerosis. I. Clinical results of a multicenter, randomized, double-blind, placebo-controlled trial. *Neurology* 1993; 43: 655-661., K.P. Johnson et al. Copolymer 1 reduces relapse rate and improves disability in relapsing-remitting multiple sclerosis: Results of a phase III multicenter, double-blind, placebo-controlled trial. *Neurology* 1995; 45: 1268-1276.

**FTY720 Phase II study results** L. Kappos et al. Promising results with a novel oral immunomodulator FTY720 in relapsing MS. Clinical Abstract of data presented at the 21st Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS)/10th Annual Meeting of the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) meeting, Thessalonica, Greece, Sept 28-Oct 1, 2005., P. O Connor et al. Phase II study with oral FTY720 in relapsing MS: Results of the dose-blinded active drug extension phase at 12 months. Clinical Abstract of data presented at the 21st Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS)/10th Annual Meeting of the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) meeting, Thessalonica, Greece, Sept 28-Oct 1, 2005.

The results are from a large Phase II study conducted at 32 centers in 11 countries (Europe and Canada). In the initial, placebo-controlled part of this study, 281 patients were randomized in equal numbers to receive either placebo, 1.25 mg or 5.0 mg FTY720 orally once-daily for six months. The study evaluated the effect of FTY720 on disease activity as measured by MRI and clinical relapses as well as its tolerability and safety. After six months, patients in the placebo group were re-randomized to receive either FTY720 1.25 mg or 5 mg blinded for an additional six months, while patients already on FTY720 continued their originally-assigned treatment. A total of 98% of the 255 patients who completed the first six months volunteered to continue in the extension phase evaluating the longer-term effects of FTY720.

In the 12-month analysis, both patient groups on FTY720 (1.25 mg and 5 mg) who had experienced a reduction in their annualized relapse rate of more than 50% during the first six months compared to placebo maintained this low relapse rate during the subsequent six-month extension. In those patients who switched from placebo to either 1.25 mg or 5 mg of FTY720 after six months, the annualized relapse rate was reduced by at least 70% during the second six-month study phase compared to the first six months on placebo.

The MRI results at 12 months showed low levels of inflammatory disease activity in all FTY720 groups. In patients who switched from placebo to FTY720, the mean number of inflammatory (Gd-enhancing) lesions on MRI (at the 12th month) was reduced by more than 80% compared to the sixth month. More than 80% of patients who received FTY720 for up to 12 months were free from lesions showing active inflammation on MRI at the 12th month irrespective of their FTY720 treatment dose (1.25 mg or 5 mg).

FTY720 appeared to be well tolerated, with 91% of patients who entered the extension phase completing the 12th month on the study drug. There were no unexpected safety findings during the extension as compared to the six-month placebo-controlled phase. The most frequently reported adverse events in patients treated up to twelve months were non-serious infections (colds, influenza), headache, diarrhoea and nausea.

#### **About FTY720**

Oral FTY720 has a novel mode of action different from all available therapies. It reversibly sequesters lymphocytes away from blood and susceptible target organs such as the central nervous system (CNS), thereby reducing neuroinflammation in MS. FTY720 has been developed by Novartis Pharma and licensed from Mitsubishi Pharma Corporation.



## About Multiple Sclerosis

MS is the most common inflammatory and neurodegenerative disorder of the central nervous system, including the brain, spinal cord and optic nerves. Multiple Sclerosis International Federation ([http://www.msif.org/en/ms\\_the\\_disease/index.html](http://www.msif.org/en/ms_the_disease/index.html)) MS typically presents itself in relapsing forms. The relapsing-remitting (RRMS) course is the most common form of the disease. Patients suffer acute self-limiting attacks (relapses) of neurological dysfunction followed by complete or incomplete remission in function. Over time, transmission of electrical nerve impulses is disrupted, nerve cells are destroyed, and patients experience symptoms ranging from fatigue, tingling, numbness and blurred vision to poor muscle control with partial or complete paralysis, speech or mental impairment. About 50% of patients advance to the secondary progressive (SPMS) course within 10 years. Weinshenker BG. Natural history of multiple sclerosis. *Ann Neurol* 1994, 36: S6-S11.

This release contains certain forward-looking statements relating to Novartis' business, which can be identified by the use of forward-looking terminology such as "suggest", "expected to be launched", "will be confirmed" or similar expressions, or regarding potential future revenue from FTY720. Such forward-looking statements reflect the current views of Novartis 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 any indications or labeling in any market. Nor can there be any guarantee of potential future sales of FTY720. Neither can there be any guarantee regarding the long-term impact of a patient's use of FTY720. In particular, management's expectations regarding commercialization of FTY720 could be affected by, among other things, unexpected clinical trial results; unexpected regulatory actions or delays or government regulation generally; Novartis' ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry and general public pricing pressures, 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 has been a leader in the neuroscience area for more than 50 years, having pioneered early breakthrough treatments for Alzheimer's disease, Parkinson's disease, attention deficit/hyperactivity disorder, epilepsy, schizophrenia and migraine. Novartis continues to be active in the research and development of new compounds, is committed to addressing unmet medical needs and to supporting patients and their families affected by these disorders.

Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2004, the Novartis group of companies' businesses achieved sales of USD 28.2 billion and pro forma net income of USD 5.8 billion. The group invested approximately USD 4.2 billion in R&D. Headquartered in Basel, Switzerland, Novartis group companies employ about 83,700 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

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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: November 1, 2005

By: /s/ MALCOLM B. CHEETHAM

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