

NOVARTIS AG  
Form 6-K  
September 29, 2006

## 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 dated September 28, 2006

(Commission File No. 1-15024)

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### Novartis AG

(Name of Registrant)

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Switzerland

(Address of Principal Executive Offices)

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Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

**Form 20-F:** ☒ **Form 40-F:** ☐

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Yes: ☐ **No:** ☒



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- Investor Relations Release -

**Novartis seeks European approval for Rasilez® to become the first in a new class of medicines to help patients with high blood pressure**

- *Direct renin inhibitors expected to be the first new class of high blood pressure medicines available in more than 10 years*
- *Rasilez shows significant double-digit blood pressure reductions when used alone and significant additive reductions when added to other blood pressure medicines*
- *New clinical data show Rasilez also provides rapid onset of action, 24-hour blood pressure control maintained over time and placebo-like safety and tolerability*

**Basel, September 28, 2006** Rasilez® (aliskiren), a new medicine that would represent the first new treatment approval for people with high blood pressure in more than a decade, has been submitted for European Union approval.

The submission, which was accepted by the European Medicines Agency (EMA), includes data from more than 7,800 patients with high blood pressure taking Rasilez in 44 clinical trials. These results show Rasilez produces sustained double-digit reductions in blood pressure, reaches its maximal lowering effect within four weeks, and has placebo-like safety and tolerability within the expected therapeutic dose range.

In addition to being effective by itself as a monotherapy, Rasilez further reduces blood pressure when co-administered with many common anti-hypertension therapies, including angiotensin converting enzyme inhibitors (ACE inhibitors), calcium channel blockers (CCBs) or the diuretic hydrochlorothiazide (HCTZ).

High blood pressure and its consequences is the world's No. 1 killer and is estimated by the American Heart Association to affect one in four adults around one billion people globally(1), (2), (3). Despite extensive use of current therapies, about 70% of all people with high blood pressure do not reach their target blood pressure levels(4). Many patients require three or more medicines to control their blood pressure(5). Meanwhile, many existing treatments fail to provide sustained 24-hour blood pressure control, particularly during the early morning hours.

Rasilez, which was developed in collaboration with Speedel AG, is a first-of-its-kind treatment resulting from the long search for effective renin inhibition through an oral medicine. It acts within the renin system, which is central to blood pressure regulation. By suppressing the renin system's point of activation renin Rasilez decreases the activity of this system, as measured by plasma renin activity (PRA)(6).

Physicians and patients need new therapeutic approaches for controlling blood pressure and its associated complications. We've been hoping for a direct renin inhibitor for long time, said Professor Roland Schmieder, Department of Nephrology and Hypertension at the University of Erlangen-Nürnberg in Germany. Data on aliskiren show that directly inhibiting renin can provide the control our patients need and might provide other long-term benefits.



The most recent clinical data, which was presented in September, highlighted the power of Rasilez to maintain its 24-hour blood pressure lowering over one year of therapy and to continue its lowering effects for up to four weeks after the medicine was stopped(7).

Throughout the clinical program, Rasilez has consistently shown tolerability comparable to placebo at doses up to 300 mg daily. Rasilez has also been well-tolerated when used alone or with other common cardiovascular and anti-diabetic medicines.

For more than 40 years, medical researchers have focused on controlling over-activation of the renin system, said James Shannon, MD, Global Head of Development at Novartis. As a direct renin inhibitor, Rasilez has the potential to redefine how high blood pressure is treated. We intend to conduct a large clinical program involving more than 40,000 patients to evaluate the potential long-term benefits of Rasilez beyond blood pressure control.

In April 2006 the US Food and Drug Administration (FDA) accepted aliskiren for regulatory review. Submissions in other markets are planned.

#### **Disclaimer**

The foregoing release contains forward-looking statements which can be identified by the use of terminology such as intend, seeks, expected to be, would represent, might provide, potential, estimated, or similar expressions, or by express or implied discussions regarding potential future regulatory filings, approvals or future sales of Rasilez. Such statements reflect the current views of the Novartis group of companies with respect to future events and are subject to certain risks, uncertainties and assumptions. There can be no guarantee that Rasilez will be approved for sale in any market, or that it will reach any particular sales levels. In particular, management's expectations regarding the approval and commercialization of Rasilez could be affected by, among other things, unexpected clinical trial results, including additional analysis of existing clinical data and new 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; increased 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 AG (NYSE: NVS) is a world leader in offering medicines to protect health, treat disease and improve well-being. Our goal is to discover, develop and successfully market innovative products to treat patients, ease suffering and enhance the quality of life. Novartis is the only company with leadership positions in both patented and generic pharmaceuticals. We are strengthening our medicine-based portfolio, which is focused on strategic growth platforms in innovation-driven pharmaceuticals, high-quality and low-cost generics, human vaccines and leading self-medication OTC brands. In 2005, the Group's businesses achieved net sales of USD 32.2 billion and net income of USD 6.1 billion. Approximately USD 4.8 billion was invested in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 97,000 people and operate in over 140 countries around the world. For more information, please visit <http://www.novartis.com>.

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**New data for FTY720 aiming to become the first orally effective multiple sclerosis treatment show sustained benefits over two years**

- *Phase II results show sustained reduction in relapses and inflammation in MS patients, with low disease activity maintained over two years*(1)
- *International Phase III clinical trials now under way, with plans to involve more than 3,000 patients*
- *FTY720 may represent a new approach to treating multiple sclerosis (MS) through its unique mode of action*
- *MS the most common disorder of the central nervous system in young adults, affecting more than 2.5 million people worldwide*(2)

**Basel, September 28, 2006** The developmental oral therapy FTY720 (fingolimod) has demonstrated sustained benefits over two years in patients suffering from relapsing multiple sclerosis (MS), indicating that it could provide an important new option for treating this disabling neurological disease estimated to affect more than 2.5 million people worldwide.

New Phase II data presented today show that up to 77% of patients taking once-daily FTY720 remained free of relapses over two years. They also maintained a low rate of inflammatory disease as measured by magnetic resonance imaging (MRI)(1).

The results were presented at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) meeting in Madrid. They provide longer-term data regarding the clinical profile of FTY720 following the publication of one-year Phase II data in the *New England Journal of Medicine* on September 14, 2006(3).

New preclinical data also presented at the congress suggest that FTY720 may work through multiple modes of action. In addition to its anti-inflammatory effects, preclinical data suggest that FTY720 may have the potential to reduce neurodegeneration and enhance repair of the central nervous system affected by MS(4), (5), (6).

MS is a progressive and debilitating disorder of the central nervous system (CNS) that frequently affects young people, women twice as often as men. It is the most common inflammatory and neurodegenerative disorder of the CNS, causing problems with muscle control and strength, vision, balance, sensation, and mental functions(3). MS typically presents in relapsing forms involving acute self-limiting attacks of neurological dysfunction (or relapses ) followed by complete or partial restoration of functions.

The results presented at ECTRIMS are very promising, and if confirmed by Phase III data, FTY720 could contribute significantly to improving the quality of life of patients with relapsing MS, said Professor Ludwig Kappos, chief trial investigator and head of the Outpatient Clinics Neurology-Neurosurgery at the University Hospital in Basel. The data show that FTY720 may offer important clinical benefits. In addition, it is given conveniently in the form of a once-daily pill.

Conventional first-line therapies for MS offer an average reduction in relapse rates in the range of 30-35% in two-year studies. These medicines require frequent injections, ranging from daily to weekly, and are often associated with skin reactions at the site of the injection(7), (8), (9).

### **FTY720 a new approach to treating MS**

FTY720, the first oral sphingosine 1-phosphate receptor (S1P-R) modulator, may represent a new approach to the treatment of MS through its unique mode of action.

In MS, inflammatory lymphocytes (T-cells) are believed to be responsible for the destruction of the protective myelin coating which surrounds the nerves in key areas of the brain and spinal cord. This destruction hinders the ability of nerves to send electrical signals, resulting in problems with muscle movement, coordination, balance and cognition.

FTY720 binds to the sphingosine 1-phosphate receptor-1 (S1P1) on circulating lymphocytes and reversibly traps a proportion of them in the lymph nodes. As a result, FTY720 lowers the number of activated T-cells circulating in the bloodstream and central nervous system. Preclinical data suggest that FTY720 may also impact the neurodegenerative component of MS and promote endogenous repair.

FTY720 has been developed by Novartis and licensed from Mitsubishi Pharma Corporation.

### **Phase III clinical trials underway**

The positive Phase II results support further evaluation of FTY720 through a large-scale program of Phase III studies in relapsing-remitting MS, which started earlier this year.

This includes a Phase III clinical trials program called FREEDOMS (FTY720 Research Evaluating Effects of Daily Oral therapy in Multiple Sclerosis). This randomized, double-blind, placebo-controlled study program is planned to include over 2,000 patients worldwide aged 18-55 with the relapsing-remitting form of MS. Study participants will be randomized equally to either receive once-daily oral treatment with FTY720 1.25 mg or 0.5 mg or placebo for a period of 24 months.

Novartis has also initiated a 12-month, international, randomized, double-blind study with more than 1,000 patients called TRANSFORMS (Trial Assessing injectable interferon  $\beta$  vs FTY720 Oral in RRMS) comparing once-daily oral treatment with FTY720 1.25 mg or 0.5 mg to interferon beta-1a injected once-weekly.

### **Details of new Phase II data**

The data presented at ECTRIMS are from an 18-month active drug extension of a core six-month placebo controlled study in patients with relapsing MS. The results show that at six months, FTY720 reduced inflammatory disease activity as seen on MRI by up to 80%, and relapse rate by more than 50%, compared to placebo. In the extension phase, placebo patients were switched to active therapy(1).

Over two years of FTY720 treatment, MRI and clinical disease activity remained low, resulting in an annualized relapse rate of 0.2 with up to 77% of patients remaining relapse-free. More than 80% of patients were free from lesions showing active inflammation on MRI. Patients who received placebo for the first six months also experienced a marked improvement after switching to FTY720, and the improvement was sustained through month 24(1).

The large-scale study was conducted at 32 centers in 11 countries in Europe and Canada. In the initial placebo-controlled phase, 281 patients were randomized equally to receive FTY720 (1.25 mg or 5 mg) or placebo once-daily for six months(3). Of the 255 patients who completed this part of the study, 98% volunteered to continue in the extension phase. Patients in the placebo group were then re-randomized to receive either 1.25 mg or 5 mg of FTY720 in a dose-blinded manner. Those already on FTY720 continued with their original treatment.

In the six-month placebo-controlled phase of the study, the most frequent adverse events reported for FTY720 were dose-dependent upper respiratory tract infections (mainly nasopharyngitis) and dyspnea, plus diarrhea and nausea(3). FTY720 treatment was associated with initial dose-dependent decreases in heart rate and expiratory air flow. Clinically asymptomatic increases in alanine aminotransferase (liver enzyme) and an increase in blood pressure were also observed. No unexpected adverse events emerged in patients treated for up to 24 months compared with the six month placebo-controlled phase(3). There was no further elevation



of blood pressure with continued treatment beyond the effect seen at six months. The ongoing Phase III study program includes comprehensive monitoring, which will provide further characterization of the safety profile of FTY720.

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This release contains certain forward-looking statements relating to the business of Novartis, which can be identified by the use of forward-looking terminology such as potential, may offer, may represent, may impact, could change, could contribute, or similar expressions by express or implied discussions regarding potential future regulatory submissions or approvals or regarding potential future revenue from fingolimod. 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 fingolimod to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that fingolimod will be submitted for approval or will be approved for sale for any indications or labeling in any market. Nor can there be any guarantee that fingolimod will achieve any sales or any particular level of sales. In particular, management's expectations regarding fingolimod could be affected by, among other things, unexpected clinical trial results, including additional analysis of existing clinical data or new clinical data; 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, and 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 offering medicines to protect health, treat disease and improve well-being. Our goal is to discover, develop and successfully market innovative products to treat patients, ease suffering and enhance the quality of life. Novartis is the only company with leadership positions in both patented and generic pharmaceuticals. We are strengthening our medicine-based portfolio, which is focused on strategic growth platforms in innovation-driven pharmaceuticals, high-quality and low-cost generics, human vaccines and leading self-medication OTC brands. In 2005, the Group's businesses achieved net sales of USD 32.2 billion and net income of USD 6.1 billion. Approximately USD 4.8 billion was invested in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 97,000 people and operate in over 140 countries around the world. For more information, please visit <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: September 28, 2006

By: /s/ Malcolm B. Cheetham

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Title: Head Group Financial  
Reporting and Accounting