

NOVARTIS AG  
Form 6-K  
October 03, 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 September 2005

(Commission File No. 1-15024)

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**Novartis AG**

(Name of Registrant)

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Enclosures:

1. FDA advisory committee votes unanimously to recommend approval of Exjade® for once-daily oral treatment of chronic iron overload due to blood transfusions (Basel, September 30, 2005)
  
2. New data show that Novartis indacaterol provides 24-hour efficacy with single dose in patients with asthma and COPD  
(Copenhagen, September 19, 2005)
  
3. Three-year study confirms long-term benefits of Xolair® for patients with severe allergic asthma  
(Basel, September 19, 2005 )
  
4. Novartis signs global licensing agreement to develop new topical applications of terbinafine the most prescribed oral treatment for fungal nail infections (Basel, September 15, 2005)
  
5. Sandoz Files Lawsuit Seeking FDA Ruling on Omnitrope  
(Holzkirchen, Germany, September 13, 2005)
  
6. Novartis and Alnylam create major alliance to discover RNAi therapeutics  
(Basel, Switzerland, and Cambridge, MA, September 7, 2005)
  
7. New data demonstrate benefits of Diovan® in reducing life-threatening complications from narrowed arteries after a heart attack (Stockholm, September 5, 2005)

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**MEDIA RELEASE**

**COMMUNIQUE AUX MEDIAS**

**MEDIENMITTEILUNG**

**FDA advisory committee votes unanimously to recommend approval of Exjade® for once-daily oral treatment of chronic iron overload due to blood transfusions**

*Novel, once-daily oral iron chelator may eliminate need for lengthy, burdensome infusion with current standard of care*

*Committee supports use of Exjade in patients age 6 and older*

*Review is based on data from largest global clinical trials program of its type, including 1,000+ adults and children*

**Basel, September 30, 2005** Novartis announced today that the Blood Products Advisory Committee (BPAC) of the U.S. Food and Drug Administration (FDA) gave a positive review of Exjade® (deferasirox).

Exjade is currently under priority review by the FDA as the first and only once-daily oral iron chelator for the treatment of chronic iron overload due to blood transfusions in adults and children. A newly designed molecule, Exjade is administered as a once-daily drink after tablet(s) are dispersed in a glass of water or orange juice.

The committee unanimously voted to recommend approval for use of Exjade for patients with chronic iron overload due to blood transfusions. The FDA generally follows the recommendations of its advisory committees, although it is not obligated to do so. If approved, Exjade may be a major advance in iron chelation therapy in the U.S.

We believe the Blood Products Advisory Committee has recognized the potential of Exjade to dramatically improve the management of patients with transfusional iron overload, said Diane Young, MD, vice president, global head, Clinical Development, Novartis Oncology. During the next several weeks we will work closely with the FDA to answer any remaining questions, in hopes of bringing this new treatment option to patients

as soon as possible.

Exjade, which has been designated an orphan drug in both the EU and the US, is currently under priority review in the US, Canada, Switzerland, Australia and New Zealand. Additional regulatory submissions have been filed around the world.

Iron overload is a cumulative, potentially life-threatening, unavoidable consequence of frequent blood transfusions used to treat certain rare, chronic blood disorders, including thalassemia, sickle cell disease, other rare anemias and myelodysplastic syndromes. Signs of iron overload may be

detected after 10 to 20 blood transfusions. If left undiagnosed or untreated, the excess iron in the body leads to damage to the liver, heart and endocrine glands. Iron chelation has been demonstrated to be the only effective treatment for transfusion-related iron overload.

### **Filing Data**

The Exjade filings were based on the results of a pivotal clinical trials program, including a Phase III head-to-head trial vs. Desferal® (deferrioxamine), which showed that Exjade significantly reduced liver iron concentration (LIC) at doses of 20-30 mg/kg/day. These clinical trials, which included more than 1,000 adults and children, were part of the largest prospective global clinical trials program ever implemented for an investigational iron chelator. LIC is the accepted indicator for body iron content in patients receiving blood transfusions. The studies demonstrated that Exjade at 20-30 mg/kg/day led to the maintenance or reduction of iron burden in transfused patients with thalassemia, sickle cell disease, other rare anemias and myelodysplastic syndromes. In the clinical studies, Exjade was generally well tolerated, with the most frequently reported adverse events being nausea, vomiting, diarrhea, abdominal pain, skin rash and increases in serum creatinine. As with deferrioxamine, cases of ocular and auditory disturbances have been reported.

### **About Iron Chelation**

In iron chelation an agent binds to iron in the body and helps remove it through the urine and/or feces. To date, only deferrioxamine is globally available for the first-line treatment of transfusional iron overload. While deferrioxamine is effective, it typically requires subcutaneous infusion lasting eight to twelve hours per day, for five to seven days a week for as long as the patient continues to receive blood transfusions or has excess iron within their body. In many patients the need for transfusions may be life-long. However, due to the inconvenience and discomfort associated with the administration of deferrioxamine, many patients choose not to undergo iron chelation therapy, exposing themselves to the dangers of iron overload. Novartis believes the approval of Exjade would, therefore, not only help patients currently receiving iron chelation, but also extend the benefits of iron chelation to those not currently undergoing therapy.

### **Additional Information**

Clinical trials with Exjade are ongoing. To learn more about Exjade clinical trials, health care providers can call either 800 561 1376 in the US, or +44 (0) 1506 814899 outside the US.

The foregoing release contains forward-looking statements that can be identified by terminology such as if approved, Exjade may be , believes, potential, will, in hopes of bringing, would, dramatically improve, recommended, or similar expressions, or by express or implied discussion regarding potential marketing approvals or future sales of Exjade. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Exjade to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Exjade will receive any marketing approvals, or that it will reach any particular sales levels. In particular, management's expectations regarding commercialization of Exjade could be affected by, among other things, additional analysis of Exjade clinical data; new clinical data; unexpected clinical trial results; 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 U.S. 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.

For prescribing information on Desferal (deferoxamine) please contact your local Novartis affiliate.

**About Novartis**

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 a 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 approximately 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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**MEDIA RELEASE      COMMUNIQUE AUX MEDIAS      MEDIENMITTEILUNG**

**New data show that Novartis indacaterol provides 24-hour efficacy with single dose in patients with asthma and COPD**

*Studies confirm indacaterol could become first in new class of once-daily beta2-agonists*

**Copenhagen, September 19, 2005** Novartis announced today that its development compound indacaterol demonstrated effective and well-tolerated treatment of asthma and chronic obstructive pulmonary disease (COPD) over 24 hours with a rapid onset of action, according to new data presented at the congress of the European Respiratory Society (ERS) in Copenhagen, Denmark.

The combination of 24-hour efficacy and a reassuring safety profile suggests that in time, a once-daily dose of indacaterol could become a new standard of care for bronchodilation in asthma and COPD, said Joerg Reinhardt, Global Head of Development, Novartis Pharma AG. We are now concentrating on the development of this important new therapy for the benefit of patients who suffer from these debilitating and sometimes fatal diseases.

The results of a series of clinical studies presented at the meeting show that indacaterol (formerly known as QAB149) could become the first in a new class of once-daily beta2-agonists, offering potential therapeutic benefits for patients with asthma and COPD. Indacaterol could be the first beta2-agonist to be taken only once-daily providing full 24 hour symptom control with a single administration, in contrast to currently-available long-acting beta2-agonists (LABAs) such as salmeterol and formoterol which have to be taken twice-daily.

Key indacaterol data presented at ERS included those demonstrating its 24-hour bronchodilator efficacy in COPD, as well as in asthma. Even at high doses, indacaterol demonstrated a good overall safety profile with no concerns over key adverse events sometimes associated with beta2-agonists. These data reinforce the results of preclinical studies.

Considered together, these results provide important insights into the future therapeutic potential of indacaterol, the first in a new generation of drugs that could accurately be described as once-daily beta2-agonists, said Prof. Stephen Holgate, Southampton General Hospital, UK. For patients with asthma or COPD, indacaterol could provide important clinical benefits in terms of improved compliance and more rapid and reliable long-term control of the potentially life-threatening symptoms of breathlessness and bronchial constriction associated with these

conditions.

**24-hour efficacy in asthma and COPD**

The efficacy of indacaterol in both asthma and COPD was demonstrated in a series of placebo-controlled

clinical studies using once-daily doses of indacaterol ranging from 25 to 2000 µg.(1)-(7) The duration of action of indacaterol was found to be largely independent of dose, with superior bronchodilation to placebo demonstrated at 24 hours after a single dose.(1)

The efficacy of indacaterol in patients with asthma was further investigated in three multiple-dose studies of 7, 14 and 28 days duration.(3)-(5) In these studies, the 24-hour bronchodilator efficacy of indacaterol observed on the first day was maintained for the duration of the studies, suggesting that regular use of indacaterol is not associated with the development of tolerance, or tachyphylaxis. Indacaterol also demonstrated 24-hour bronchodilator efficacy with no evidence of tachyphylaxis in patients with COPD.(6),(7)

### **Strong safety profile**

Data presented at ERS demonstrate that the 24-hour efficacy of indacaterol in asthma is accompanied by a positive safety profile. Single indacaterol doses up to 2000 µg were well-tolerated and were not associated with any clinically significant changes in known class effect adverse events such as hypokalaemia, hyperglycaemia, increased heart rate or altered QTc interval.(1),(2)

These single-dose results were confirmed in multiple-dose asthma studies, in which indacaterol doses up to 800 µg once-daily for up to 28 days were associated with a good cardiovascular safety profile and no clinically relevant effects on blood pressure, QTc, glucose or potassium levels.(3)-(5)

The positive safety profile of indacaterol in asthma was also observed in patients with COPD, at doses up to 800 µg for up to 28 days.(6),(7)

### **Findings supported by preclinical data**

Data from preclinical studies were presented at ERS and confirmed the results of clinical studies, with indacaterol acting as a potent beta2-agonist and displaying high intrinsic efficacy in isolated human bronchial tissue.(8) In other studies, indacaterol demonstrated a sustained duration of action in isolated human bronchial tissue(9) and in guinea pigs.(10) Preclinical data also support the lack of tachyphylaxis observed in clinical studies.(11)

The safety of indacaterol was also examined in the preclinical development programme. In a series of *in vitro* and *in vivo* studies, the safety of indacaterol was compared with that of two long-acting beta2-agonists (formoterol and salmeterol) in doses providing equivalent degrees of bronchodilation.(12) Indacaterol demonstrated a better cardiovascular safety profile than formoterol and salmeterol.(12) Importantly, studies using isolated human bronchial tissue suggest that indacaterol will not antagonise the bronchorelaxant effect of short-acting beta2-agonists, and therefore should not interfere with rescue medication use.(8)

### **About indacaterol**

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Indacaterol (previously known as QAB149) works by stimulating beta2-receptors in the smooth muscle of the airways. This causes relaxation of the muscle, thereby increasing the diameter of the airways, which become constricted in asthma and COPD.

Indacaterol is being developed both as monotherapy and as a fixed-dose combination with drugs such as NVA237, a long-acting anti-muscarinic agent for the treatment of COPD which has also been shown to be effective over 24 hours after a single dose.(13)

### **About asthma and COPD**

Asthma is a major, chronic airway disorder that is a serious public health problem in many

countries, and can have severe sometimes fatal consequences.(14) Asthma is one of the most common chronic diseases worldwide, affecting more than 300 million people(15) of whom an estimated 15 million suffer from severe disease.(16) Their health and quality of life are often severely affected, and more than 180,000 people worldwide are believed to die from asthma each year.(17)

COPD is also a major cause of chronic morbidity and mortality throughout the world, with many people dying prematurely from the disease or its complications.(18) COPD is currently the fourth leading cause of death in the world, and further increases in its prevalence can be predicted in the coming decades.(18) It is estimated that COPD is prevalent in 4% of the population in the USA, Europe and Japan,(19),(20),(21) and at least 15% of smokers will go on to develop the disease.(18) COPD, which encompasses chronic bronchitis and emphysema or both conditions, progresses slowly and eventually leads to a largely irreversible loss of lung function.

The foregoing press release contains forward-looking statements that can be identified by the use of forward-looking terminology such as could become, future therapeutic potential, should not, or similar expressions, or by express or implied discussions regarding the potential development and commercialization of indacaterol and NVA237. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that the agreement that is the subject of this release will lead to commercialization of indacaterol or NVA237 in any market. Any such commercialization can be affected by, among other things, uncertainties relating to product development and clinical trials; regulatory actions or delays or government regulation generally; the ability to obtain or maintain patent or other proprietary intellectual property protection and 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 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 this information as of this date and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

## About Novartis

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**MEDIA RELEASE      COMMUNIQUE AUX MEDIAS      MEDIENMITTEILUNG**

**Three-year study confirms long-term benefits of Xolair® for patients with severe allergic asthma**

**Basel, September 19, 2005** New long-term data show that Xolair® (omalizumab), a first-in-class monoclonal antibody for treating severe allergic asthma, helped patients to maintain control of their disease and was safe and well-tolerated in studies lasting more than three years. The data were presented today at the European Respiratory Society (ERS) congress in Denmark, along with results from seven clinical studies showing that Xolair significantly improved the lung function of patients.

Long-term control of severe allergic asthma was demonstrated in a study spanning 180 weeks of observation. The design included a 32-week randomised, double-blind, parallel-group, placebo-controlled study, followed by a 96-week open-label extension and a further 52-week extension.

As a result, patients completing the study and both extensions had been treated for more than three years. Disease control was maintained throughout the follow-up period in Xolair patients, who exhibited lower than expected changes in lung function and reduced use of inhaled corticosteroids (ICS).(1)

These results confirm that omalizumab potentially provides an important breakthrough in the fight against allergic asthma, said Prof. Marc Humbert of the Service de Pneumologie et Réanimation Respiratoire, Hôpital Antoine Bécclère, Clamart, France. Many people suffering from severe asthma have a substantially impaired quality of life and endure the constant fear that their next attack may prove fatal. By reducing exacerbations and the burden of disease, anti-IgE therapy offers a new approach to the treatment of this intractable condition.

Xolair manages asthma by targeting an underlying cause of allergic disease (up to 90% of asthma being allergic in origin).(2) It is designed to block the action of IgE, which is responsible for initiating the cascade of inflammatory symptoms such as airway constriction, mucus production, wheezing and shortness of breath. Xolair has been shown to decrease asthma exacerbations in some of the most difficult-to-treat patients whose condition remains inadequately-controlled despite the best conventional therapy, including inhaled corticosteroids, long-acting beta2-agonists and other controller medications.

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The Committee for Medicinal Products for Human Use (CHMP) recently gave a positive opinion on initial marketing authorisation for Xolair, opening the way for approval by the European Commission and for the therapy to become available in EU countries.

### **More about the three-year study demonstrating efficacy and safety**

In the 32-week placebo controlled study, 341 patients received Xolair (at least 0.016 mg/kg/IgE [IU/mL] every four weeks) or placebo. A total of 222 patients entered Extension 1 (96 weeks), 178 of whom continued into Extension 2 (52 weeks). Patients in the extensions maintained stable lung function (measured by forced expiratory volume in one second, or FEV1). Mean FEV1 was 2.24 litres at the start of Extension 1 and 2.26 litres at the end of Extension 2, indicating persistency of therapeutic benefit from Xolair. In addition, more than 80% of patients had good/excellent asthma control during the extensions. Patients receiving inhaled corticosteroids at the start of Extension 1 and remaining on the same steroid reduced their ICS use by an average of 11% between the start of Extension 1 and the end of Extension 2.

In this long-term study, the overall incidence of adverse events was similar in the Xolair and placebo groups during the 32-week placebo-controlled study and Extension 1 (i.e. approximately 80% in both groups). During Extension 2, 134 patients (75%) had at least one adverse event, most of which were mild to moderate in severity. Serious adverse events remained infrequent during the second extension (4.5%) and were deemed by the treating physician to be unrelated to Xolair.(3)

### **Improvements in lung function and quality of life**

Pooled data were also presented from seven trials in which allergic asthma patients (93% of whom had severe persistent disease) received Xolair as an add-on to inhaled corticosteroids, with or without oral corticosteroids and long-acting beta2-agonists. Out of 4,308 patients in the studies, FEV1 data were available for 3,537 patients (Xolair 2,443; control 1,094). Among Xolair recipients, 29.1% increased their FEV1 by  $\geq 200$ mL while 17.5% showed a  $\geq 200$ mL decrease. In the control group, 26.4% had a  $\geq 200$ mL increase in FEV1 and 26.1% had a  $\geq 200$ mL decrease. This equates to a net benefit of 11.6% for Xolair patients versus 0.3% for control (P<0.0001).(4)

Results from the same seven studies showed that add-on Xolair significantly improved patients' asthma-related quality of life, measured using the Juniper Adult Asthma Quality of Life Questionnaire (AQLQ). Quality of life data were available for 2,288 patients (Xolair 1,258; control 1,030). Those receiving Xolair had a mean increase of 1.01 points in their overall AQLQ score, compared to 0.67 in the control group (P<0.0001). Significantly more patients achieved a clinically meaningful improvement (i.e. an improved score of at least 0.5) in their AQLQ score from baseline in the Xolair group (66.3%) than the control group (53.2%, p<0.0001).(5)

### **Anti-IgE and severe asthma**

Xolair has been available in the US for treating moderate to severe allergic asthma since July 2003, and as of 30 June 2005 it had been prescribed to more than 45,000 patients. In July 2005 the CHMP gave a positive opinion on Xolair in the EU, and approval is expected later this year. If approved by the European Commission, Xolair will be indicated as add-on therapy to improve asthma control in adult and adolescent patients (12 years of age and above) with severe persistent allergic asthma, who had 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 is also approved in Australia, Brazil, Canada, Dominican Republic, Guatemala, Israel, New Zealand and Venezuela. It was developed under an agreement between Novartis Pharma AG, Genentech, Inc., and Tanox, Inc.

Around 300 million people worldwide have asthma,(6) and an estimated 15 million of them suffer

from a severe form of the disease.(7) Their health and quality of daily life are often severely affected, and more than 180,000 people are believed to die from asthma each year throughout the world.(8)

The potential benefits of anti-IgE therapy are already recognised 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.(9)

The foregoing release contains certain forward-looking statements that can be identified by terminology such as "potentially", "opening the way", "is expected", "will be", 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.

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(5) Beeh K-M *et al.* Omalizumab significantly improves quality of life in patients with severe persistent allergic asthma: a pooled analysis. Poster (P424) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.

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**MEDIA RELEASE      COMMUNIQUE AUX MEDIAS      MEDIENMITTEILUNG**

**Novartis signs global licensing agreement to develop new topical applications of terbinafine the most prescribed oral treatment for fungal nail infections**

**Basel, September 15, 2005** Novartis announced today that it has signed a global licensing agreement with NexMed, Inc (NASDAQ: NEXM) to develop new topical forms of terbinafine, the active ingredient in its popular Lamisil® (terbinafine tablets) treatment for fungal nail infections.

Novartis has acquired the exclusive rights to further develop and commercialize NexMed's NM100060 nail lacquer treatment for onychomycosis, which is commonly known as nail fungus, and for any other indications.

Patients and doctors have said that they want a range of effective treatment options for onychomycosis. The currently available topical treatments for nail infections, while often preferred by patients, provide often poor efficacy, leading to patient frustration and poor compliance, said Joerg Reinhardt, Head of Global Development, Novartis Pharma AG. This agreement combines Lamisil's proven track record of effectively and safely treating people with onychomycosis with the potential of meeting the needs of patients who want an effective and simple-to-use topical option for the treatment of nail infections.

NM100060 is currently in Phase I development with the active ingredient terbinafine, which is also the active ingredient in Lamisil, the most frequently prescribed treatment for fungal nail infection worldwide. Under the terms of the agreement, Novartis has acquired the exclusive worldwide rights to develop and commercialize NM100060, which incorporates NexMed's NexACT® drug delivery technology to effectively enhance penetration of terbinafine in the infected nail areas.

**More about Lamisil**

Lamisil oral tablets are the No. 1 prescribed treatment based on sales for fungal nail infections with a proven efficacy and safety profile. More than 17 million people have treated their infections with Lamisil in the US since 1996.



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Lamisil contains the active ingredient terbinafine, which inhibits production of fungal cells by disrupting the fungal cell membranes. Terbinafine travels to the infected area under the toenail or fingernail since it is also attracted to keratin, which may also disrupt the infection. Because terbinafine accumulates and lingers in the area of the nail that is growing, it can continue to work for months even after the prescription is finished, allowing the nail to heal naturally over a period of time.

### More about onychomycosis

Onychomycosis is a fungal infection affecting the toenails and/or fingernails. It is one of the most common dermatological diseases, affecting an estimated 30 million people in the US. Nail fungus can be painful, embarrassing, expensive and difficult to treat. A 1998 *American Journal of Dermatology* article estimated costs of monitoring and treatment of nail fungus ranged between USD 700 and USD 1,200 per patient annually.

The foregoing release contains forward-looking statements that can be identified by terminology such as "to develop and commercialize", "potentially meeting", or similar expressions, or by express or implied discussions regarding the potential development and commercialization of NM100060. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that the agreement that is subject of this release will lead to commercialization of NM100060 in any market. In particular, management's expectations regarding commercialization of NM100060 could be affected by, among other things, uncertainties relating to product development and clinical trials; 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; industry, government, 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 pharmaceuticals and consumer health. In 2004, the Novartis Group's businesses achieved sales of USD 28.2 billion and pro forma net income of USD 5.6 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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**MEDIA RELEASE      COMMUNIQUE AUX MEDIAS      MEDIENMITTEILUNG**

**Sandoz Files Lawsuit Seeking FDA Ruling on Omnitrope**

**HOLZKIRCHEN, Germany, September 13, 2005** Sandoz announced today that it has filed a lawsuit against the US Food and Drug Administration, seeking a ruling on its pending new drug application for the human growth hormone Omnitrope.

We believe it is important for patients and health-care providers that cost-effective follow-on protein products like Omnitrope become available as safe and effective, but less expensive and equivalent therapeutic alternatives, said Andreas Rummelt, CEO of Sandoz. Having already acknowledged the sound science behind this application, the FDA should approve Omnitrope.

Under both the Federal Food Drug and Cosmetic Act and the Food Prescription Drug User Fee Act, the FDA is required to either approve or reject new drug applications. Sandoz filed its application for Omnitrope in July 2003. On September 2, 2004, Sandoz announced that FDA had notified the company that the Agency was unable to reach a decision on whether to approve the company's application for Omnitrope. No action on the application has been taken since then.

The lawsuit, filed in US District Court for the District of Columbia, seeks to reverse the Agency's failure to act on the Omnitrope application in accordance with the Commissioner's statutory obligations.

As a Food, Drug and Cosmetic Act biologic drug, the application for Omnitrope was filed in accordance with the 505(b)(2) regulatory pathway. At the same time, Sandoz acknowledges that the approval of most follow-on protein products, licensed under the Public Health Service Act (PHS Act) in the US, will require new legislation to give the FDA the authority to approve substitutable PHS Act products. The company supports a transparent public process to design suitable legislations to help enable an appropriate regulatory pathway for follow-on protein

products, with an emphasis on ensuring patient safety while protecting legitimate intellectual property rights of innovator companies.

Follow-on protein products is the FDA's preferred term for copies of recombinant DNA-derived protein products made by companies other than the innovator and using an abbreviated approval path. These products are generally more difficult to make than traditional small-molecule generic drugs due to their greater complexity. However, using updated, state-of-the-art manufacturing and analytical processes and with an abbreviated regulatory pathway, companies like Sandoz can bring these products to market at considerable savings to patients.

**About Sandoz**

Sandoz, a Novartis company, is a world leader in generic pharmaceuticals and develops, manufactures and markets these medicines as well as pharmaceutical and biopharmaceutical active ingredients. As a Retail Generics company Sandoz is also operating a Business Unit with specific strategic focus Anti-Infectives. In 2004, Sandoz employed around 13,400 people worldwide and posted sales of USD 3.0 billion. In 2005, Novartis acquired the Generic companies Hexal AG, Germany, and Eon Labs Inc., U.S. and integrated them into Sandoz. The combined company has pro forma 2004 sales of USD 5.1 billion and more than 20,000 employees.

This release contains certain forward-looking statements which can be identified by the use of forward-looking terminology, such as *should*, *will*, *or* similar expressions, or by express or implied discussions regarding potential future regulatory approvals for Omnitrope. Such forward looking statements involve known and unknown risks, uncertainties and other factors that may cause the actual results to be materially different from any future results, performance, or achievements expressed or implied by such statements. There can be no guarantee that the lawsuit described above will be successful, or that Omnitrope will be approved for sale in the US. Management's expectations regarding Omnitrope could be affected by, among other things, uncertainties relating to the litigation process; uncertainties relating to government regulations; as well as factors discussed in Novartis AG's Form 20-F filed with the 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. Sandoz 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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**MEDIA RELEASE**

**COMMUNIQUE AUX MEDIAS**

**MEDIENMITTEILUNG**

**Novartis and Alnylam create major alliance to discover RNAi therapeutics**

**Basel, Switzerland, and Cambridge, MA, September 7, 2005** Novartis (NYSE:NVS), and Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), announced today a major multi-year alliance focused on the discovery of innovative therapeutics based on RNA interference (RNAi). The alliance will combine the research expertise and understanding of disease mechanism and pathway biology of Novartis with Alnylam's leading position in the field of RNAi.

RNAi is a natural process for selective gene silencing found in all cells. By utilizing the RNAi mechanism, RNAi therapeutics have the potential to treat human disease in a fundamentally new way through the silencing of disease-causing genes. During the term of the agreement, the collaboration will focus on the joint discovery of new therapeutics using RNAi across multiple disease areas in the Novartis research portfolio.

This collaboration underscores Novartis' commitment to forging strategic alliances with partners at the forefront of scientific discovery. RNAi holds great promise as a new therapeutic modality for treating many diseases. In particular, this exciting new area of biology has potential to target diseases that cannot be addressed by traditional approaches. This collaboration complements our robust small molecule and antibody-based research programs and will advance our efforts to develop innovative medicines for patients," said

Dr. Mark Fishman, President of the Novartis Institutes for BioMedical Research.

Novartis and Alnylam will form a Scientific Strategy and Advisory Group to review the overall strategy for the relevant science and clinical applications of the collaboration. The Advisory Group will be co-chaired by Dr. Fishman and Alnylam founder and director Phillip A. Sharp, Ph.D., Institute Professor of MIT and 1993 Nobel Laureate in Physiology or Medicine.

We believe that our technology is one of the most significant innovation-based drug discovery approaches available," said Dr. John M. Maraganore, President and Chief Executive Officer of Alnylam Pharmaceuticals. Our collaboration will utilize significant resources and capabilities to place Novartis and Alnylam in a unique position to build RNAi therapeutics as a major class of drugs in the biopharmaceutical industry.

The agreement is subject to customary regulatory approvals, including antitrust review under the Hart-Scott-Rodino Antitrust Improvements Act.

**About RNA Interference (RNAi)**

RNA interference, or RNAi, is a naturally occurring mechanism within cells for selectively silencing and regulating specific genes. Since many diseases are caused by the inappropriate

activity of specific genes, the ability to silence genes selectively through RNAi could provide a new way to treat a wide range of human diseases. RNAi is induced by small, double-stranded RNA molecules. One method to activate RNAi is with chemically synthesized small interfering RNAs, or siRNAs, which are double-stranded RNAs that correspond to a specific disease-associated gene. The siRNA molecules are used by the natural RNAi machinery in cells to cause highly targeted gene silencing.

### **Terms of the agreement**

Novartis will make initial payments of approximately \$56.8 million to Alnylam, consisting of upfront payments and the purchase of approximately 4.2 million shares of Alnylam common stock at a price of \$11.11 per share. The number of shares of Alnylam common stock to be purchased by Novartis will be determined prior to closing and will equal 19.9% of the outstanding common stock of Alnylam on the closing date. Following receipt of certain approvals, Novartis will purchase at a price of \$11.11 per share an additional number of shares of Alnylam common stock so that Novartis holds an equity interest equal to 19.9% of the total outstanding common stock of Alnylam after giving effect to the purchases by Novartis. In addition, Alnylam is eligible to receive, across multiple programs, research and early development funding, progress milestones, pre-clinical and clinical development milestones, sales milestones and royalty payments.

The collaboration agreement has an initial three-year term that may be extended for two additional one-year periods. If the collaboration is successful and multiple products are developed and commercialized, collective payments to Alnylam could exceed \$700 million, not including royalties. This figure includes payments that Alnylam would be eligible to receive if Novartis exercises a non-exclusive option to integrate Alnylam's RNAi therapeutics platform into its internal efforts, in which case Alnylam would be eligible to receive future milestones and royalties on products resulting from those efforts. Alnylam will also have an opportunity to co-invest and share profits for a defined number of products resulting from the collaboration. Alnylam retains the rights to develop its own proprietary pipeline of RNAi therapeutics, including its respiratory syncytial virus (RSV) program and other unpartnered and partnered programs, while Novartis will have a right of first offer, subject to prior agreements, should Alnylam seek additional partnerships.

### **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 5.6 billion. The Group invested approximately USD 4.2 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 81,400 people and operate in over 140 countries around the world.

For further information please consult <http://www.novartis.com>.

### **About Alnylam**

Alnylam is a biopharmaceutical company seeking to develop and commercialize novel therapeutics based on RNA interference, or RNAi. Growing from its foundation as the world's first company focused on RNAi therapeutics, the company's leadership in the field of RNAi is supported by its preeminent founders and advisors and its strengths in fundamental patents, technology, and know-how that underlie the commercialization of RNAi therapeutics. Alnylam is developing a pipeline of RNAi products using Direct RNAi to treat ocular, central nervous system, and respiratory diseases and Systemic RNAi to treat a broad range of diseases, including oncology, metabolic, and autoimmune diseases.



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The company's global headquarters are in Cambridge, Massachusetts. For additional information, please visit [www.alnylam.com](http://www.alnylam.com).

**Novartis Forward Looking Statements**

This release contains certain forward-looking statements, relating to the Company's business, which can be identified by the use of forward-looking terminology such as will be, are to be, will lead, is committed to developing, to provide, to maintain, or similar expressions by express or implied discussions regarding the potential development and commercialization of new products or regarding potential future sales from any such products. Such statements reflect the current views of the Company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. There can be no guarantee that the aforementioned research will lead to the development or commercialization of any new products in any market, or that any such products will reach any particular sales levels. Any such commercialization or sales can be affected by, among other things, uncertainties relating to product development and clinical trials, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general, as well as factors discussed in the Company's Form 20-F filed with the 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. The Company is providing this information as of this date and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

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**MEDIA RELEASE**

**COMMUNIQUE AUX MEDIAS**

**MEDIENMITTEILUNG**

**New data demonstrate benefits of Diovan® in reducing life-threatening complications from narrowed arteries after a heart attack**

*One of the largest megatrials confirms that Diovan – the most prescribed angiotensin receptor blocker – protects a broad range of people with heart disease*

**Stockholm, September 5, 2005** Diovan® (valsartan) is the first drug of its class (angiotensin receptor blocker or ARB) shown to reduce the chance of cardiovascular events that may be caused by clogged arteries (atherosclerosis) in people who have had a recent heart attack, according to data presented at the European Society of Cardiology Congress (ESC 2005).

The need for new treatments after a heart attack remains significant. More than three million people from the EU and 1.2 million people in the US suffer a heart attack every year. World Health Organization, European Health for All Database, Hospital discharges, ischemic heart disease. Available at <http://hfadb.who.dk/hfa/>, World Health Organization, International Classification of Diseases, Diseases of the Circulatory System., National Heart, Lung and Blood Institute, National Institutes of Health, Morbidity & Mortality: 2004 Chart Book on Cardiovascular, Lung, and Blood Diseases. Additionally, one in three people die within one year after their first recognized heart attack. American Heart Association, Heart Disease and Stroke Statistics – 2005 Update.

The data presented at ESC further reinforce the protective effects of Diovan, which is already the No. 1 prescribed ARB worldwide. These findings follow recent marketing authorizations throughout the world for the cardioprotective use of Diovan as a potentially lifesaving treatment for high-risk patients who have had a recent heart attack or people with heart failure. Diovan is the only ARB with both of these indications.

A new analysis of the VALIANT (VALsartan In Acute myocardial iNfarcTion) megatrial confirmed that Diovan is as effective as the ACE inhibitor captopril, a commonly used treatment, in reducing atherosclerotic events, such as heart attacks. McMurray JJ et al. The effect of valsartan, captopril, or both on atherosclerotic events after myocardial infarction: an analysis of the VALsartan In Acute myocardial iNfarcTion (VALIANT) trial; presented at ESC 2005

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Until now, the nature of ARB trials have made it difficult to determine whether this class of drugs is effective in preventing atherosclerotic events. We now have further evidence that valsartan is as effective as an ACE inhibitor in preventing atherosclerotic events, said John McMurray, MD,

Professor of Medical Cardiology and Honorary Consultant Cardiologist, Clinical Research Initiative in Heart Failure, University of Glasgow, Western Infirmary in the United Kingdom and co-principal investigator in VALIANT, in explaining the benefits of these findings for heart attack survivors.

High blood pressure is a major risk factor for cardiovascular diseases such as heart attack and heart failure. While progress has been made in treating heart attacks, people who survive the acute phase are at greatly increased risk for repeat attacks and other events that can result from clogged arteries, also called atherosclerosis. This condition is the leading cause of morbidity and mortality from cardiovascular disease and can result in heart attacks or stroke.<sup>4</sup> For example, nearly half of all heart attacks are repeat attacks,<sup>3</sup> and one in 12 men and one in nine women will have a stroke within six years of a heart attack.<sup>4</sup>

### **More on VALIANT**

The new retrospective analysis presented at ESC 2005 demonstrated similar beneficial effects of Diovan, captopril, and their combination on a composite endpoint of events that may be caused by atherosclerosis in the 14,703 patients randomized in the VALIANT trial. There was no significant difference between the effects of Diovan or captopril on the composite endpoint of cardiovascular death, heart attack, angina, revascularization, or stroke (2,175 in the Diovan group, 2,228 in the captopril group, and 2,197 in the combination group; Diovan vs. captopril  $p=0.286$ ).

VALIANT demonstrated that Diovan is the only cardiovascular agent ever shown by a head-to-head trial to be at least as effective as an ACE inhibitor in these patients. This finding can translate into a 25% reduction by Diovan in premature death in patients at high risk following a heart attack. VALIANT also showed that Diovan is well-tolerated in post-heart attack patients. The percentage of permanent discontinuations due to adverse events was statistically higher in the captopril-treated (7.7%) patients than in the valsartan-treated (5.8%) patients [ $p<0.05$ ]. Pfeffer MA, McMurray JJ et al. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med* 2003; 349(20):1893-906.

Recent regulatory approvals for Diovan in people who have had a heart attack are based on the positive results of VALIANT, one of the largest long-term studies ever conducted in people who have survived a heart attack.

### **Diovan megatrials**

A new analysis of Val-HeFT examining the protective benefits of Diovan for people with heart failure is also being presented today. Anand IS et al. Addition of an angiotensin receptor blocker to standard heart failure therapy reduces morbidity in patients with reduced renal function; abstract presented at ESC 2005 Further protective effects of Diovan have also been shown in the VALUE trial, where Diovan prevented the development of new onset diabetes compared to amlodipine. This data will be discussed at the ESC 2005 Abstract session on September 7 at 11.30 am. Kjeldsen S E. Valsartan prevents new onset diabetes compared to amlodipine in the VALUE trial; abstract presented at ESC 2005.

In order to explore this benefit of Diovan and the CV event reduction, Novartis is conducting NAVIGATOR, the largest outcomes trial ever conducted on the delay or prevention of cardiovascular events and type II diabetes in patients with impaired glucose tolerance.

Novartis is committed to improving research, especially in cardiovascular and metabolism care. The Diovan clinical trial program represents one part of this commitment, involving more than

50,000 patients across the cardiovascular continuum. Recently completed Diovan megatrials include VALUE in hypertension patients at high-risk for cardiovascular complications, VALIANT in post-heart attack patients and Val-HeFT in heart failure patients.

#### **About Diovan**

Novartis remains on the forefront of cardiovascular medicine, through development of innovative products like Diovan, the number one prescribed ARB in the world today. Diovan is available as a powerful first-line treatment for high blood pressure in more than 90 countries, for the treatment of heart attack survivors in 51 countries and in 71 countries for the treatment of people with heart failure. Additional marketing authorization applications are pending for the treatment of post-heart attack and heart failure.

For high-risk heart attack patients, Diovan recently completed the EU Mutual Recognition Procedure (MRP) in 14 countries for the treatment of clinically stable patients with symptomatic heart failure or asymptomatic left ventricular systolic dysfunction after a recent myocardial infarction.

For heart failure, Diovan also completed an EU type II variation application in 14 countries for the treatment of people with symptomatic heart failure when ACE inhibitors cannot be used, or as add-on therapy to ACE inhibitors when beta blockers can not be used.

The foregoing release contains forward-looking statements that can be identified by terminology such as potentially, are pending or similar expressions, or by express or implied discussions regarding potential new indications or labeling and marketing approvals for Diovan or regarding potential future sales of Diovan. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Diovan to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Diovan will be approved for any additional indications or labeling in any other market. Nor can there be any guarantee regarding potential future sales of Diovan. In particular, management's expectations regarding commercialization of Diovan or could be affected by, among other things, additional analysis of Diovan clinical data; new clinical data; unexpected clinical trial results; 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; industry, government, 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.

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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: October 3, 2005

By: /s/ MALCOLM B. CHEETHAM

Name: Malcolm B. Cheetham  
Title: Head Group Financial  
Reporting and Accounting